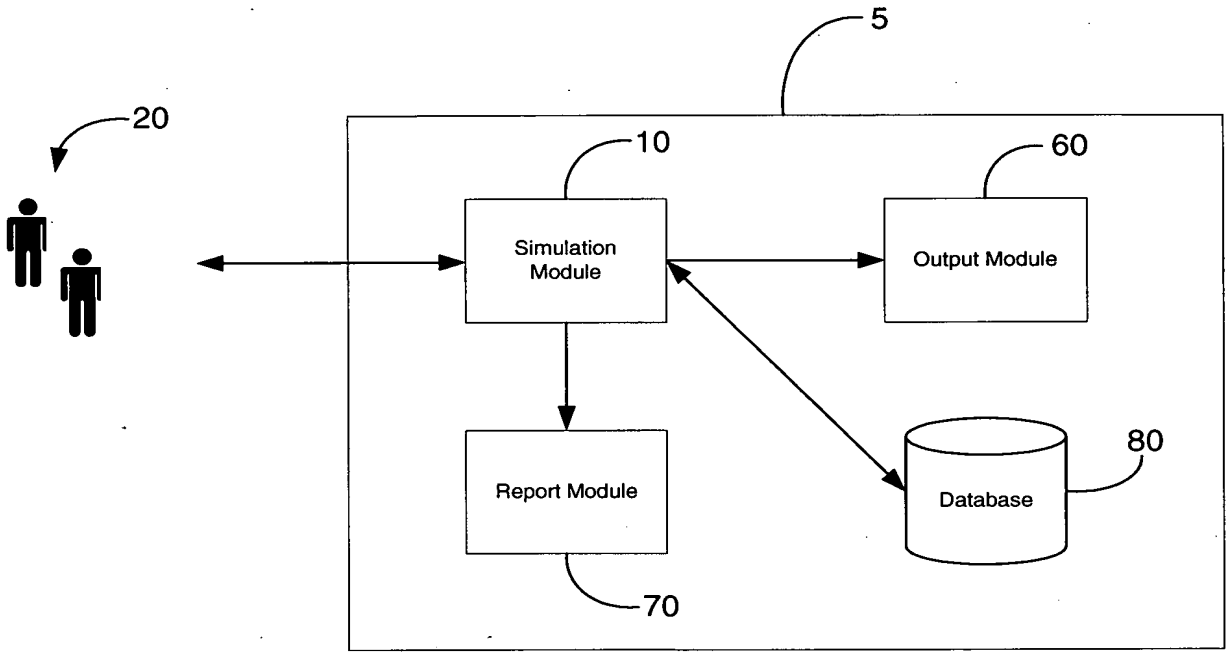

5
20
10
60
Simulation Module
Output Module
Report Module
Database
80
70

Fig. 1A

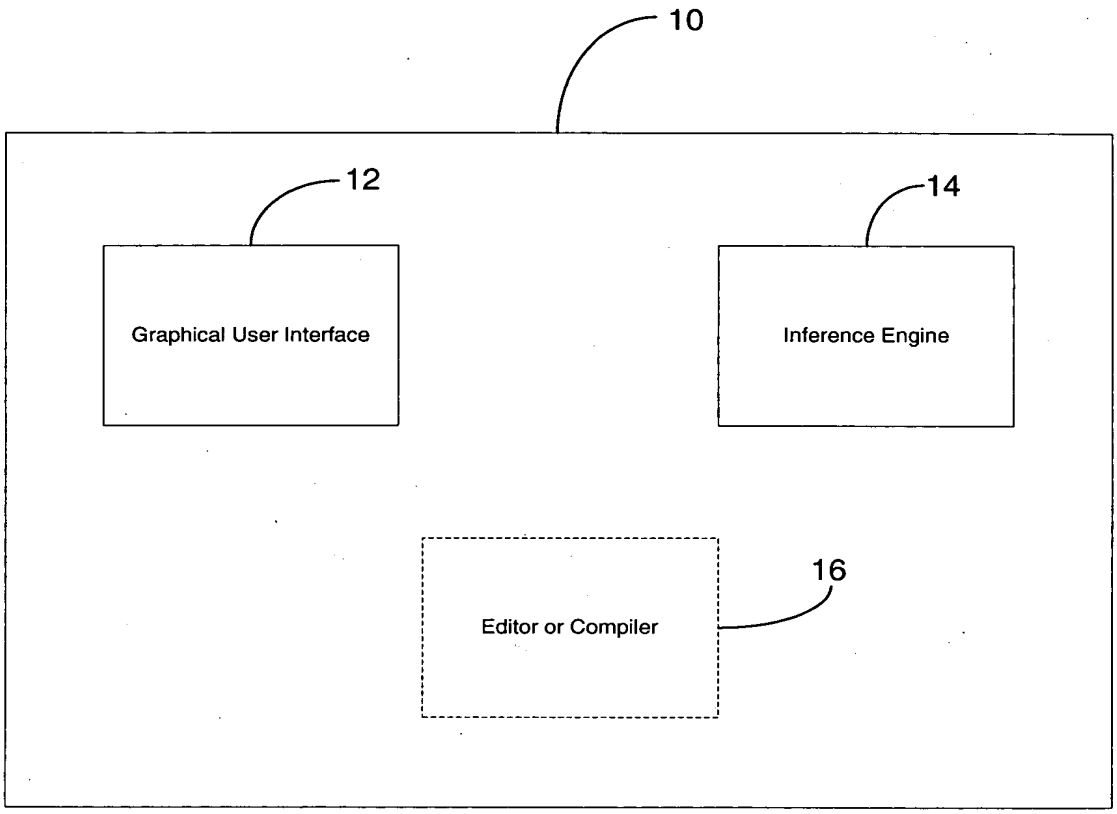
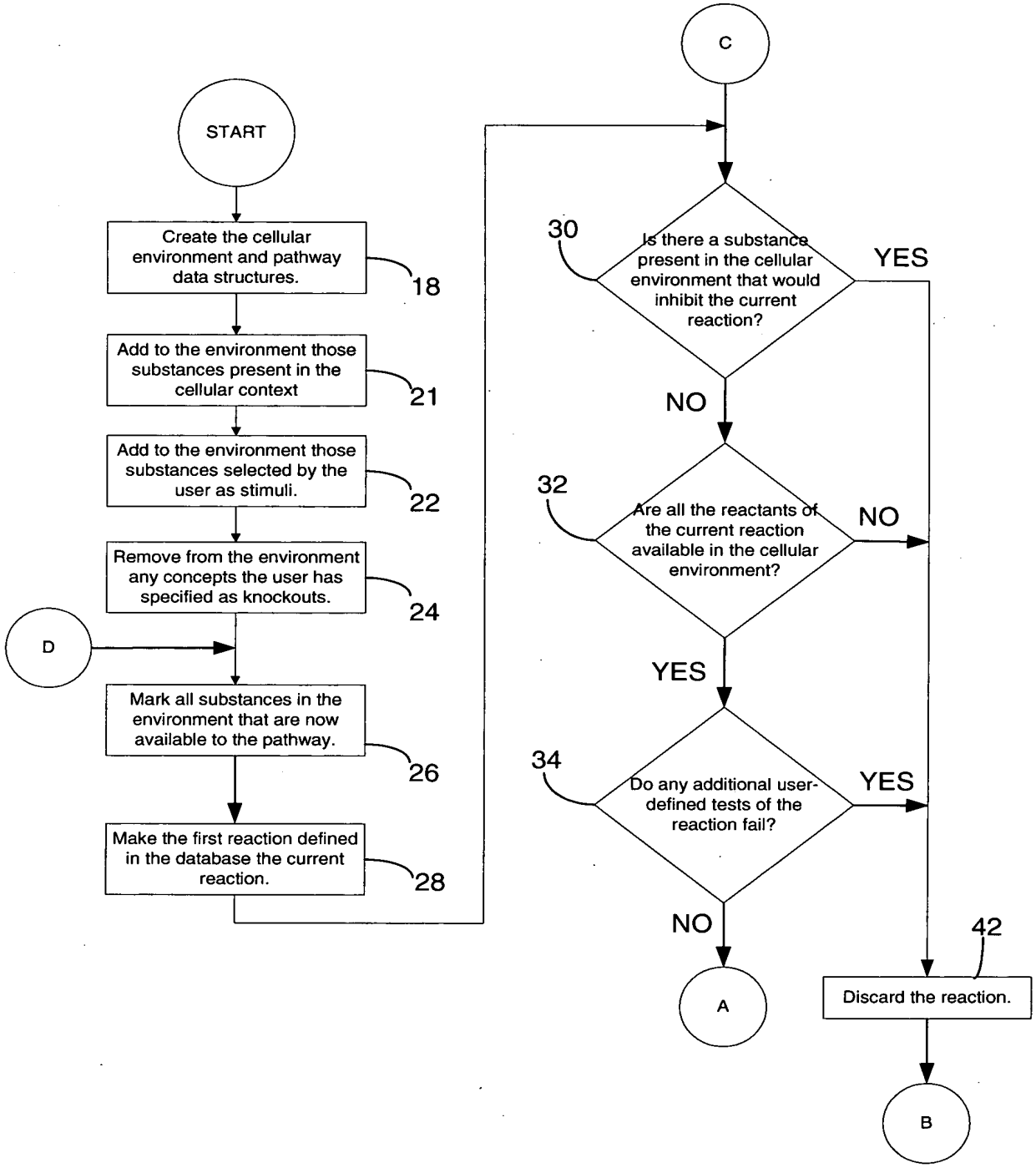

10
12
Graphical User Interface
14
Inference Engine
16
Editor or Compiler

Fig. 1B

Fig. 2A


START
Create the cellular environment and pathway data structures.
18
Add to the environment those substances present in the cellular context
21
Add to the environment those substances selected by the user as stimuli.
22
Remove from the environment any concepts the user has specified as knockouts.
24
D
Mark all substances in the environment that are now available to the pathway.
26
Make the first reaction defined in the database the current reaction.
28
C
30
Is there a substance present in the cellular environment that would inhibit the current reaction?
YES
NO
32
Are all the reactants of the current reaction available in the cellular environment?
NO
YES
34
Do any additional user-defined tests of the reaction fail?
YES
NO
A
42
Discard the reaction.
B

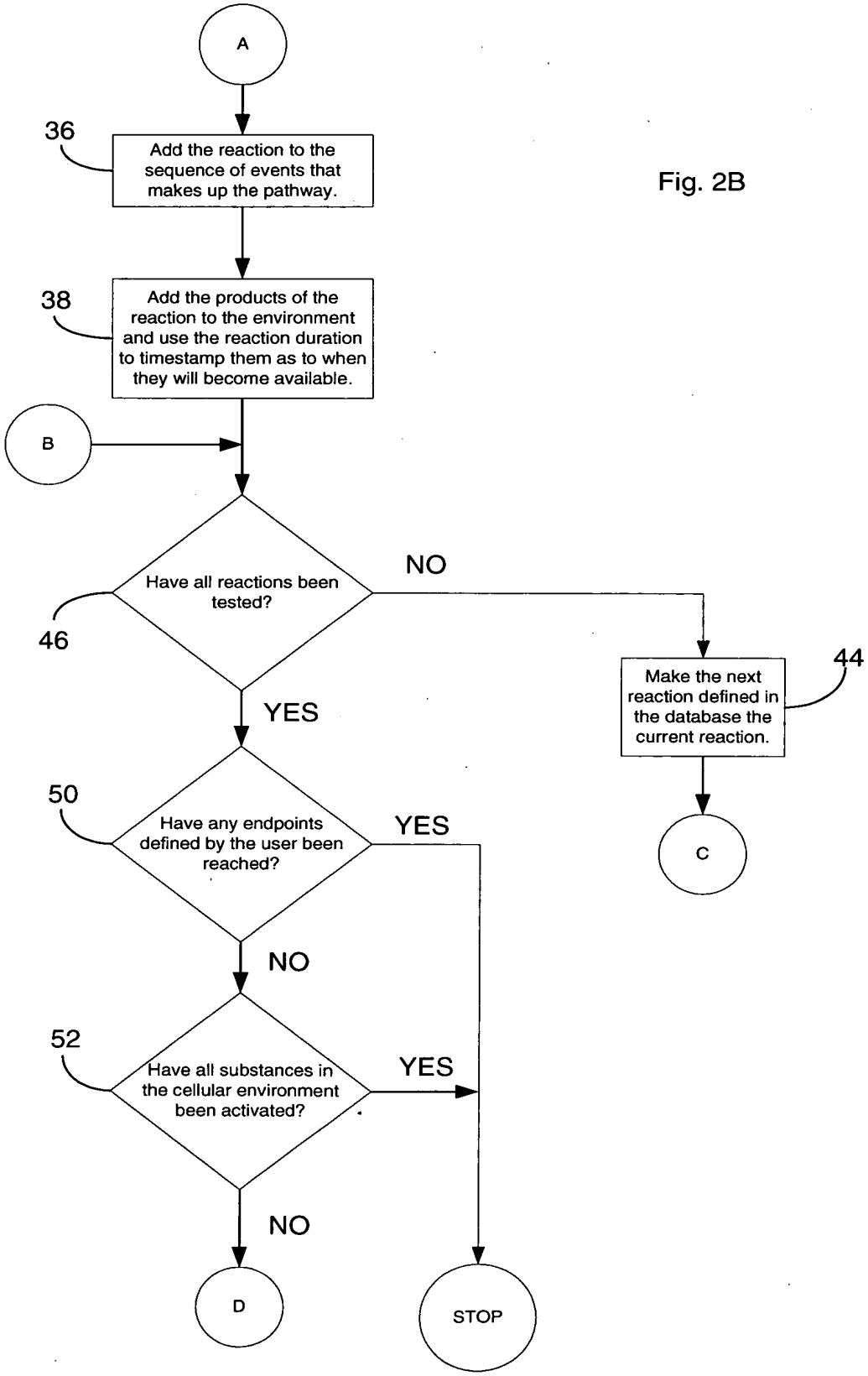

A
36
Add the reaction to the sequence of events that makes up the pathway.
38
Add the products of the reaction to the environment and use the reaction duration to timestamp them as to when they will become available.
B
Have all reactions been tested?
46
NO
YES
Make the next reaction defined in the database the current reaction.
44
C
50
Have any endpoints defined by the user been reached?
YES
NO
52
Have all substances in the cellular environment been activated?
YES
NO
D
STOP

Fig. 2B

Fig. 2C

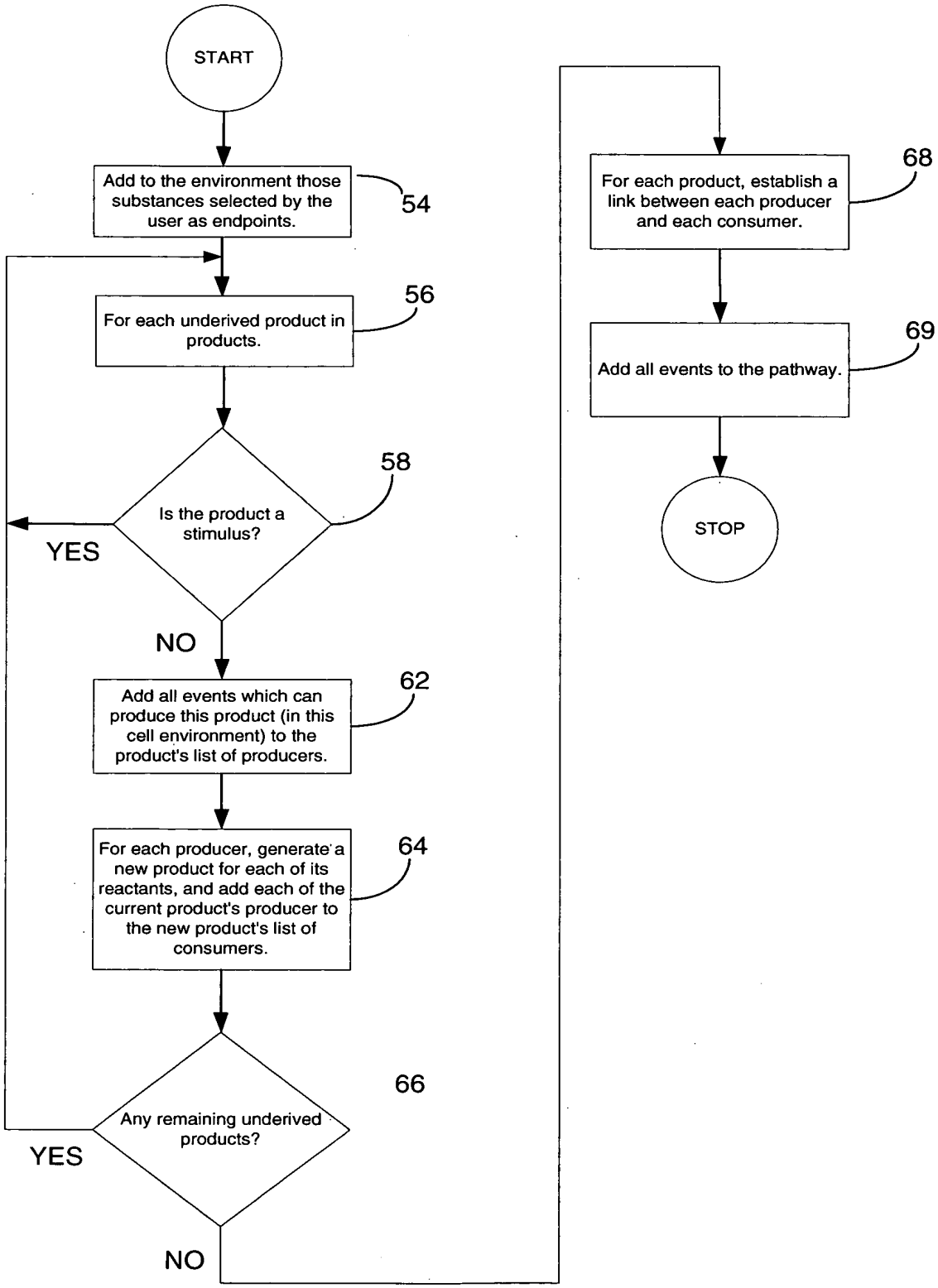

START
Add to the environment those substances selected by the user as endpoints.
54
For each underived product in products.
56
Is the product a stimulus?
58
YES
NO
Add all events which can produce this product (in this cell environment) to the product's list of producers.
62
For each producer, generate a new product for each of its reactants, and add each of the current product's producer to the new product's list of consumers.
64
Any remaining underived products?
66
YES
NO
For each product, establish a link between each producer and each consumer.
68
Add all events to the pathway.
69
STOP

FIGURE 3

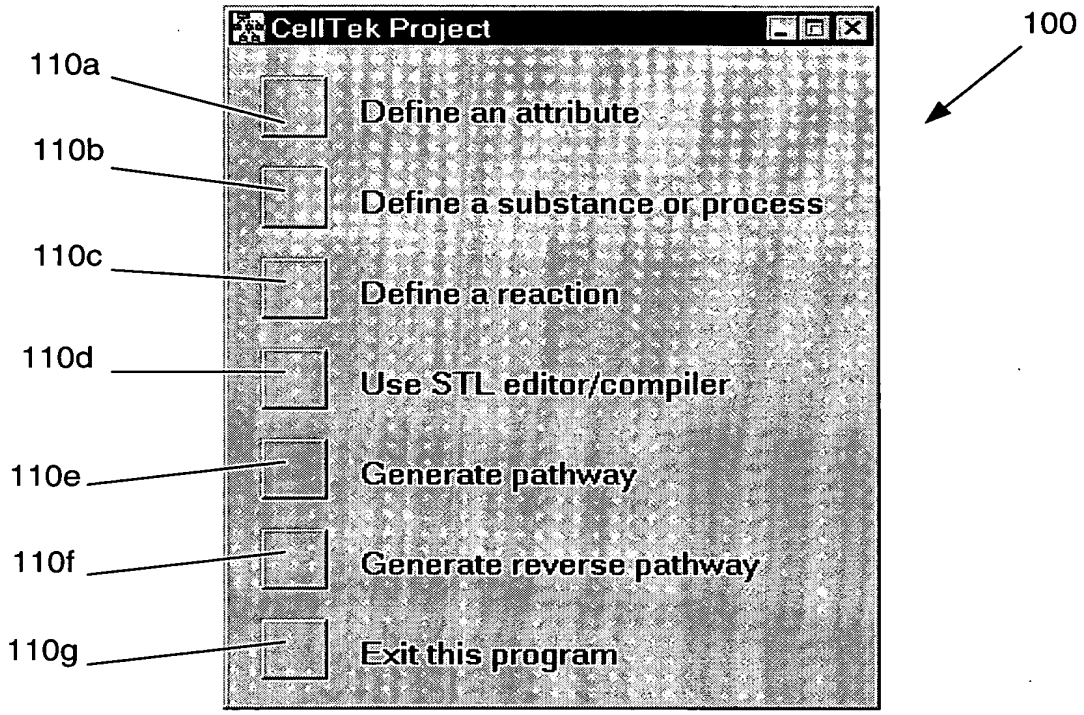


FIGURE 4A

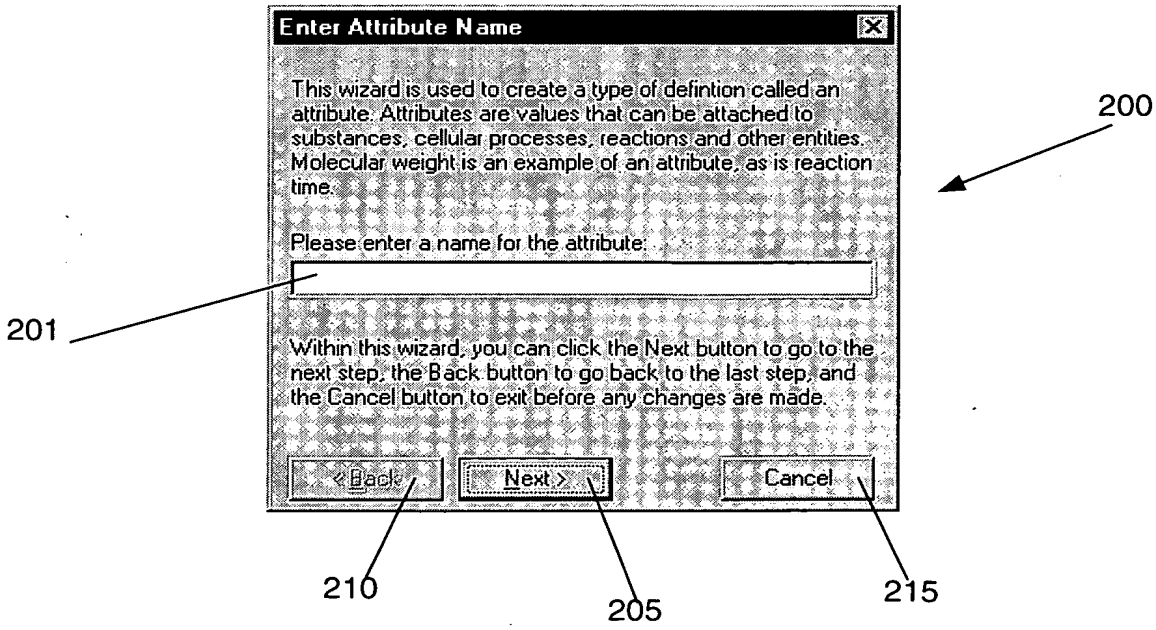


FIGURE 4B

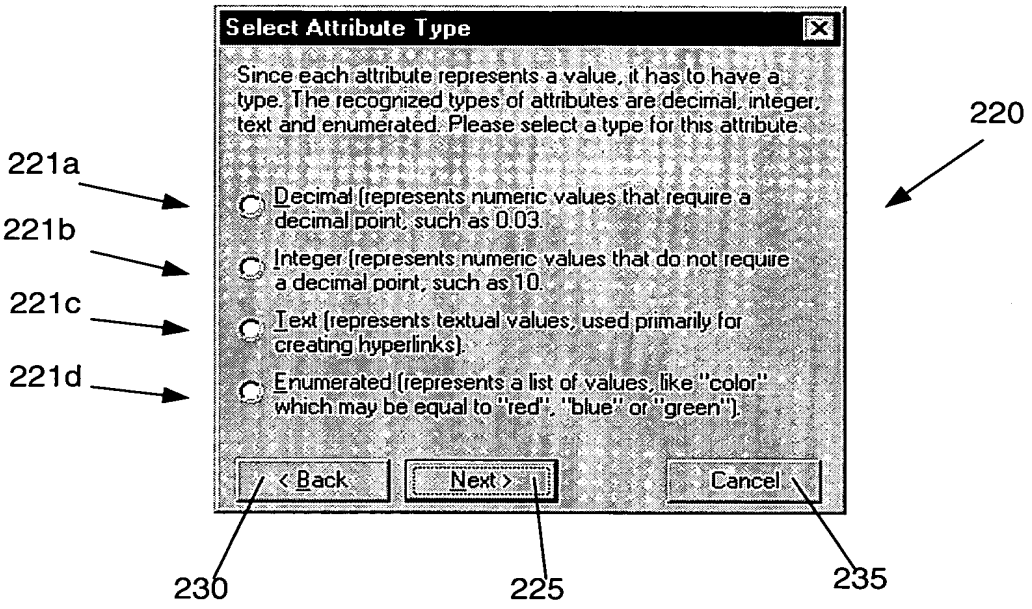


FIGURE 4C

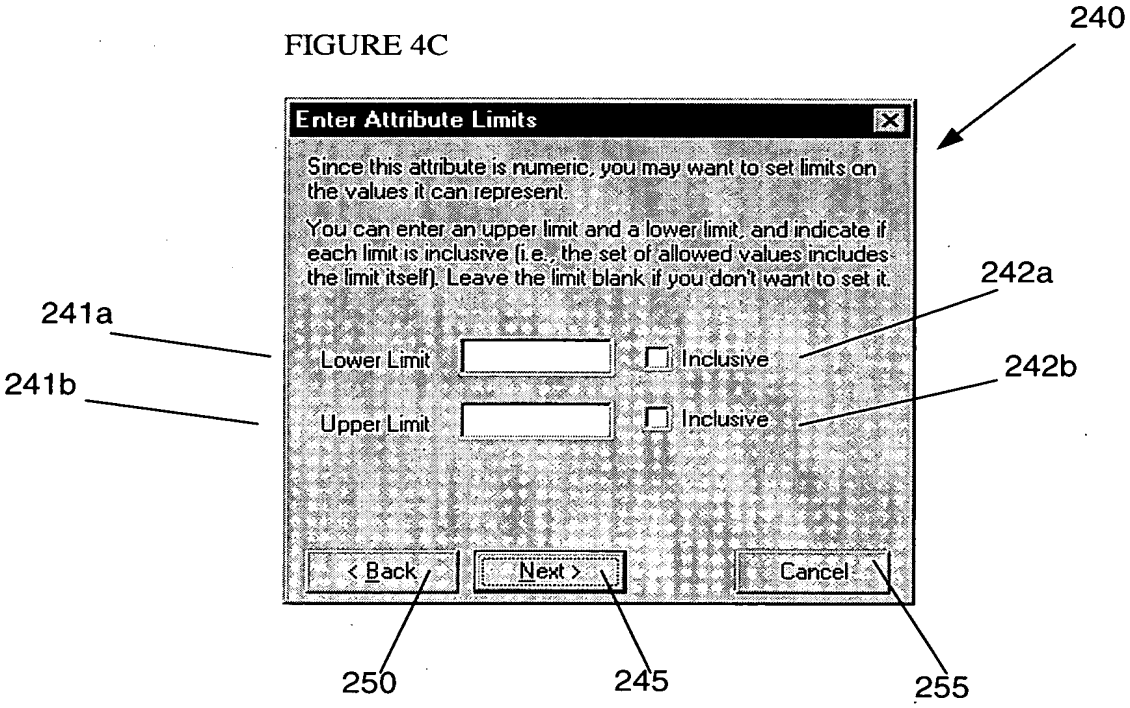


FIGURE 4D

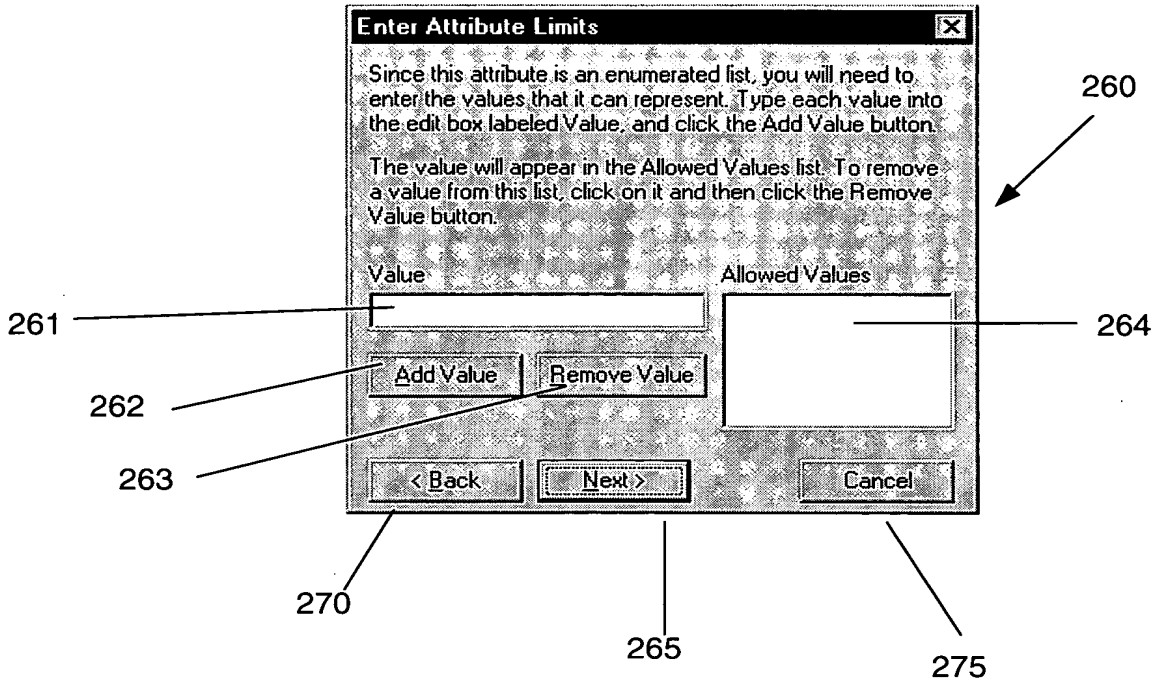


FIGURE 4E

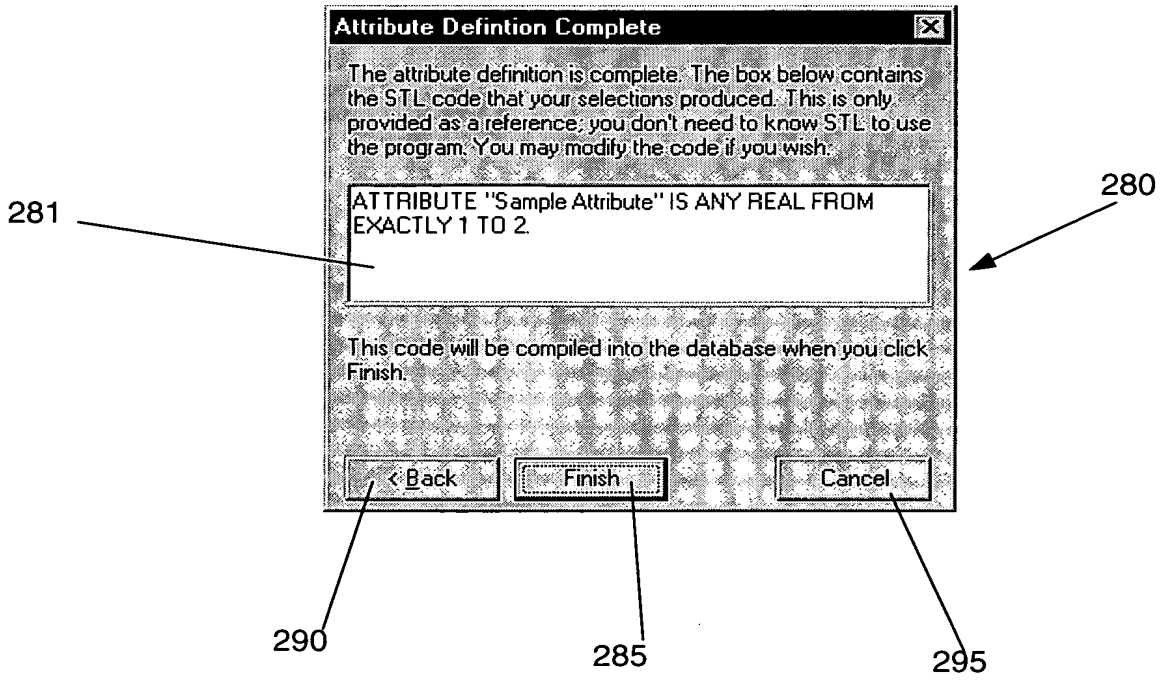


FIGURE 5A

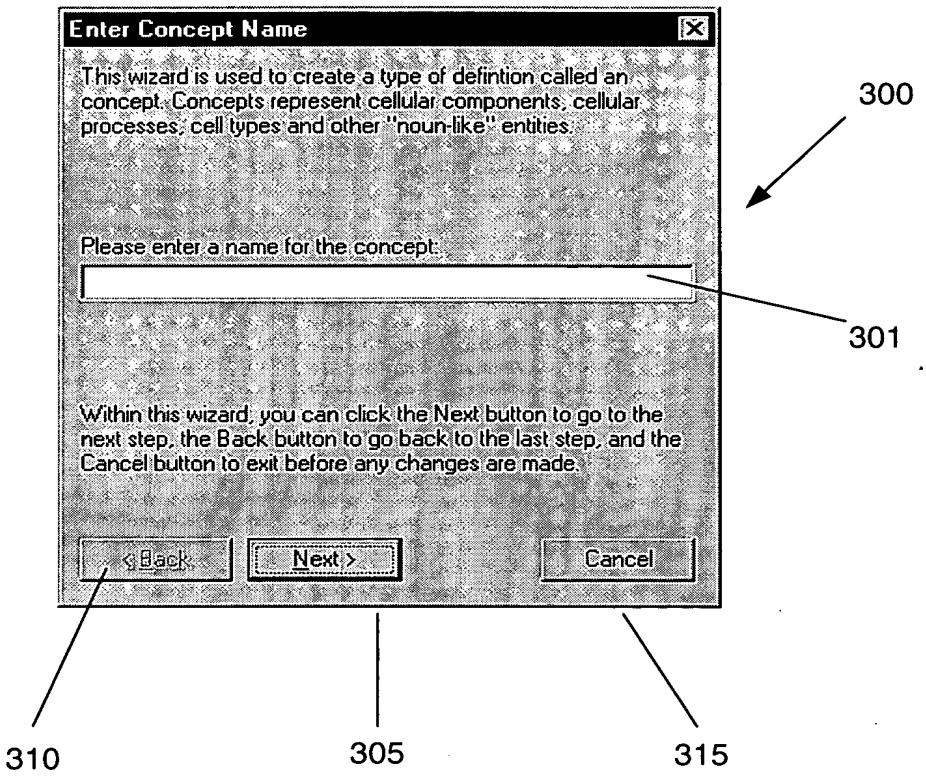


FIGURE 5B

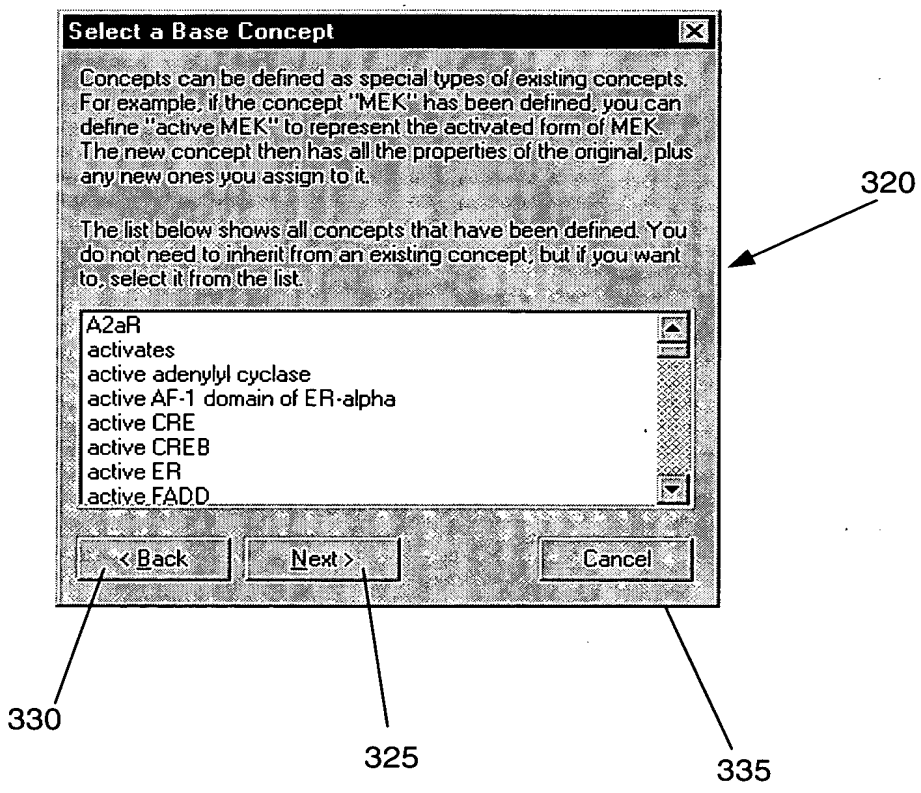


FIGURE 5C

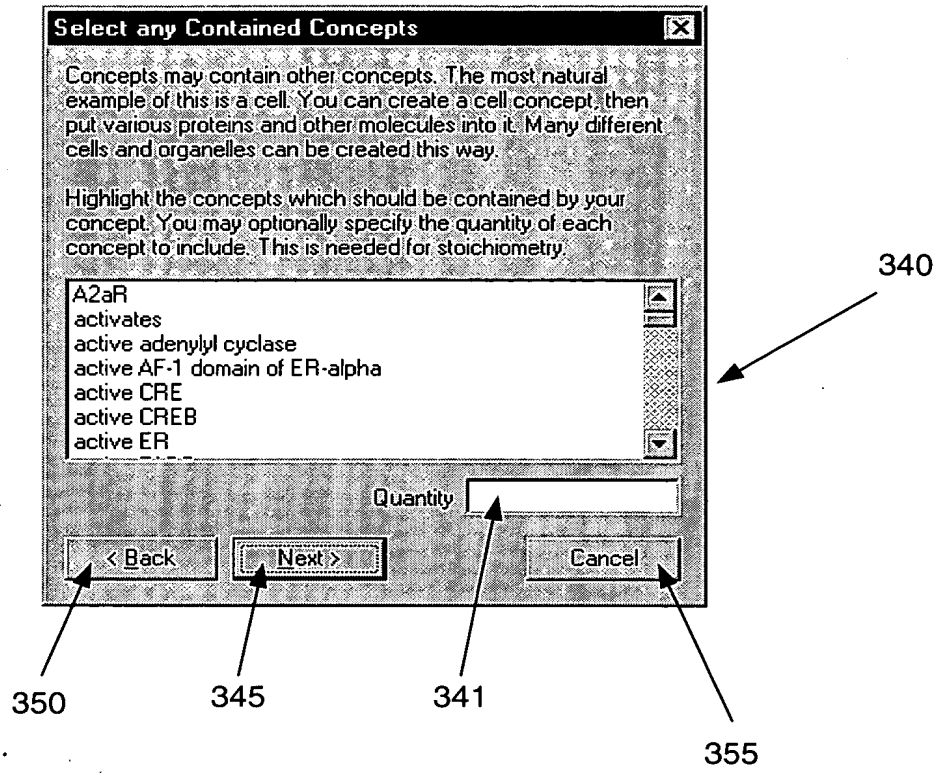


FIGURE 5D

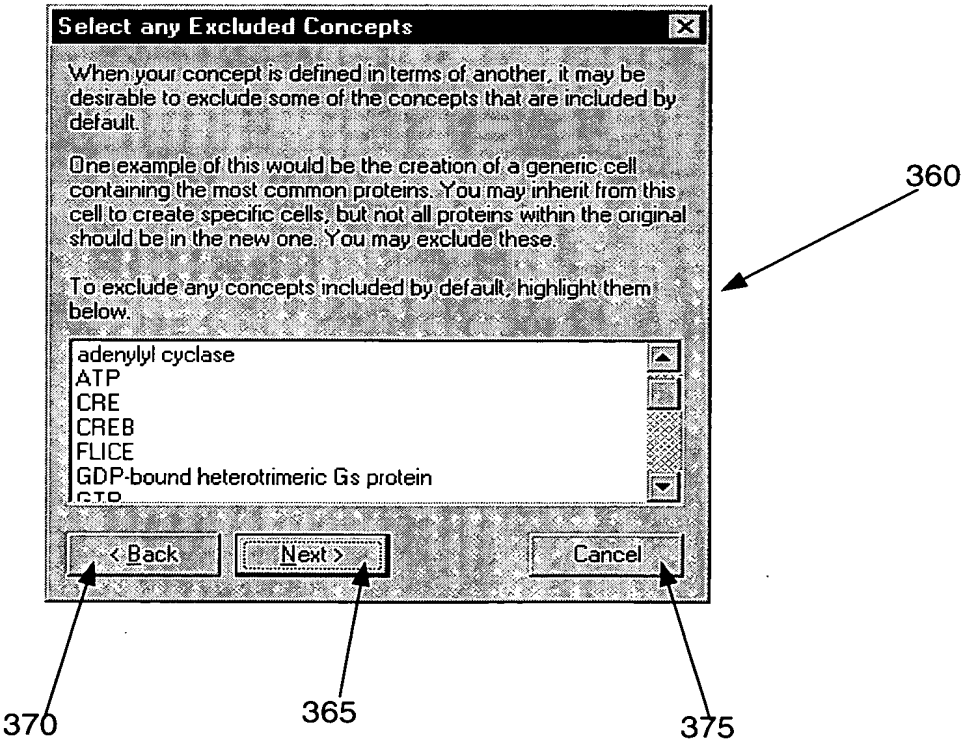


FIGURE 5E

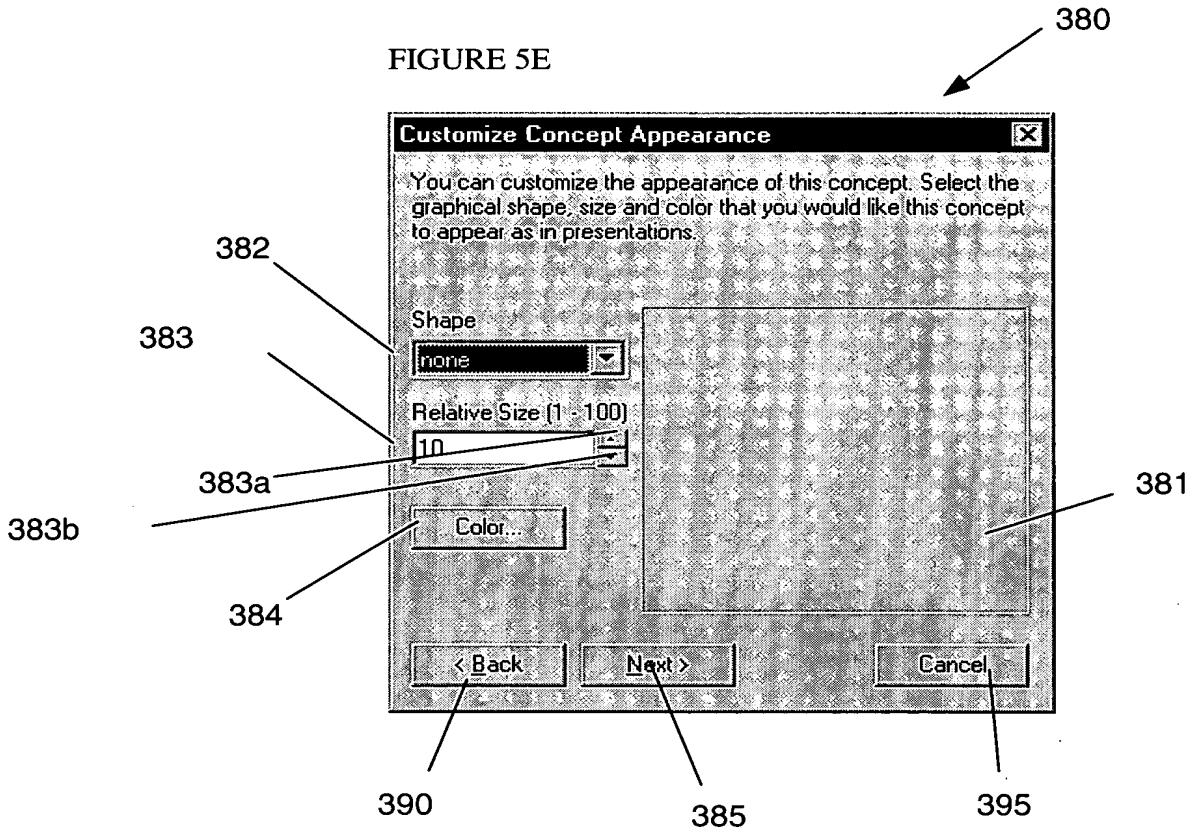


FIGURE 5F

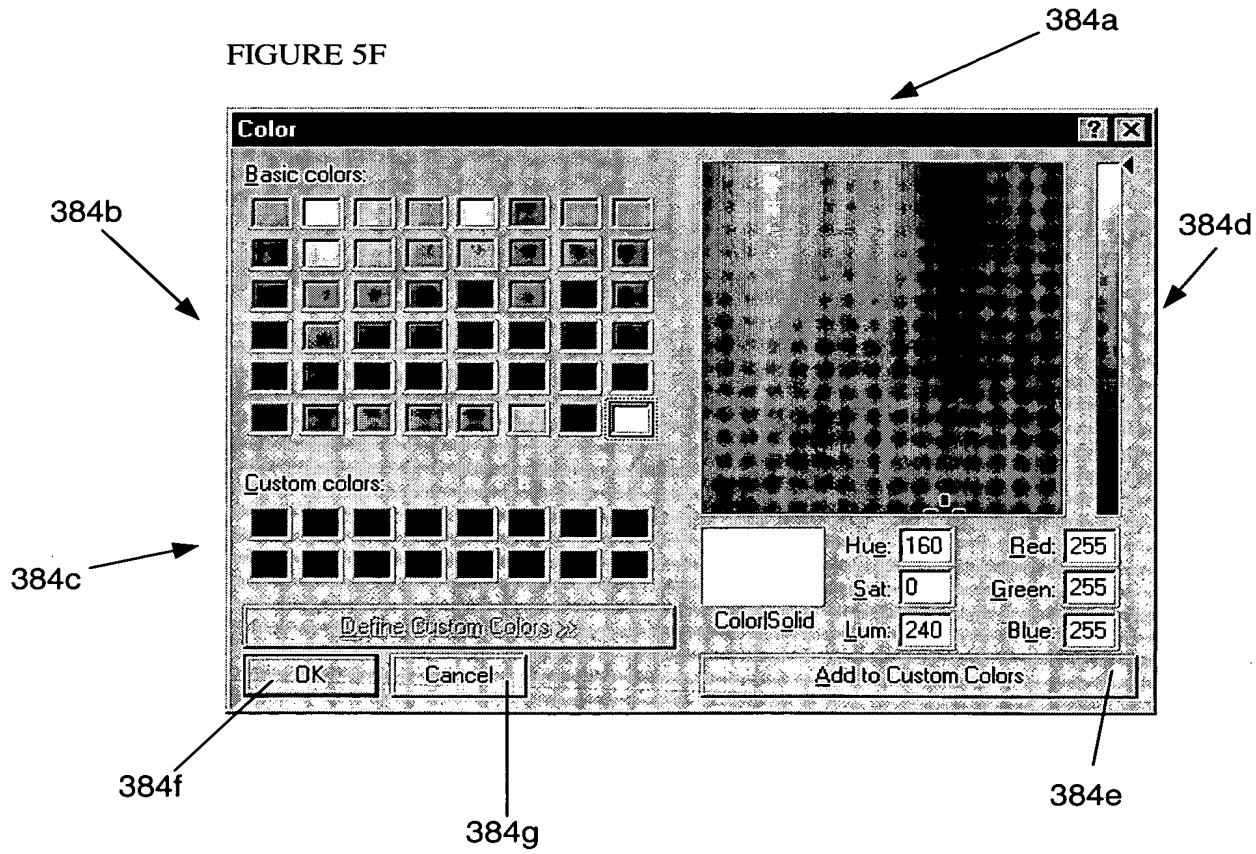


FIGURE 5G

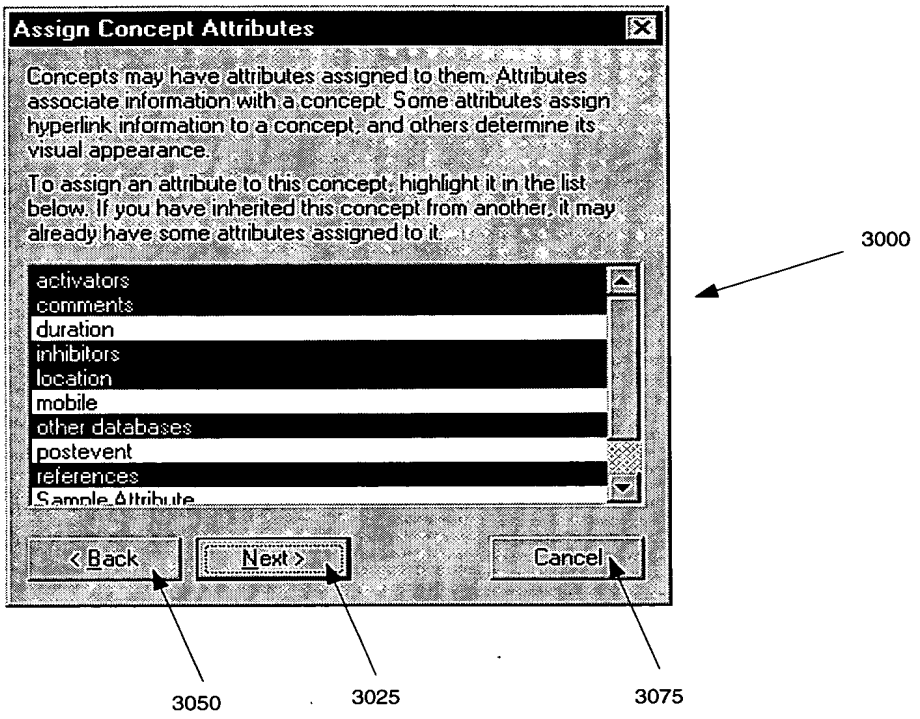


FIGURE 5H

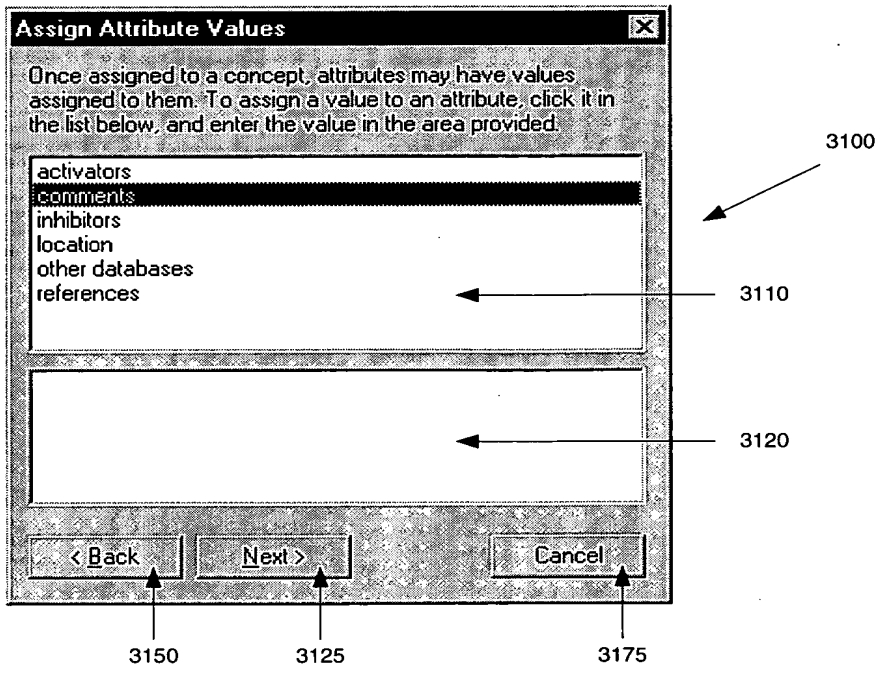


FIGURE 5I

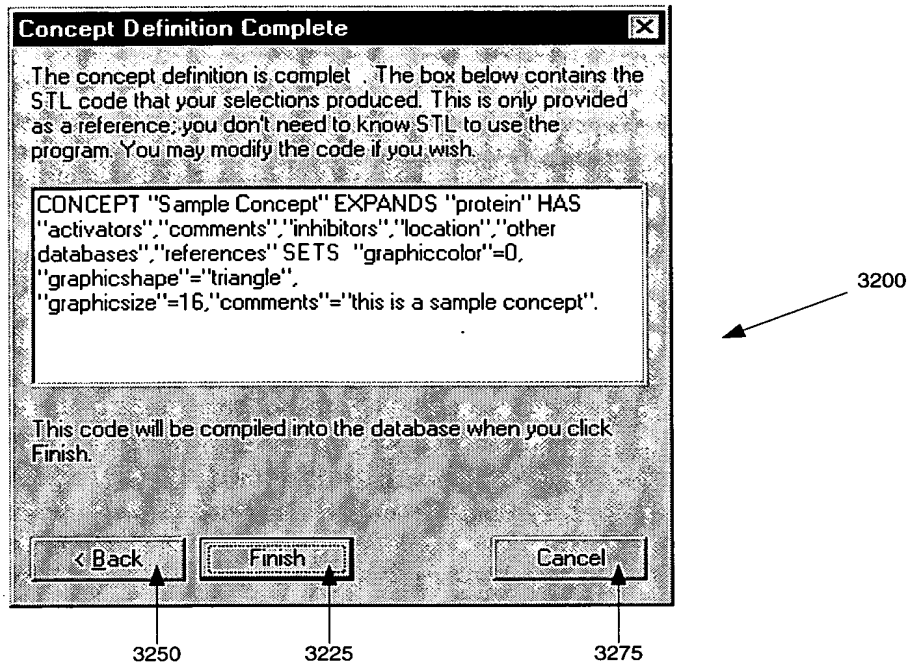


FIGURE 6A

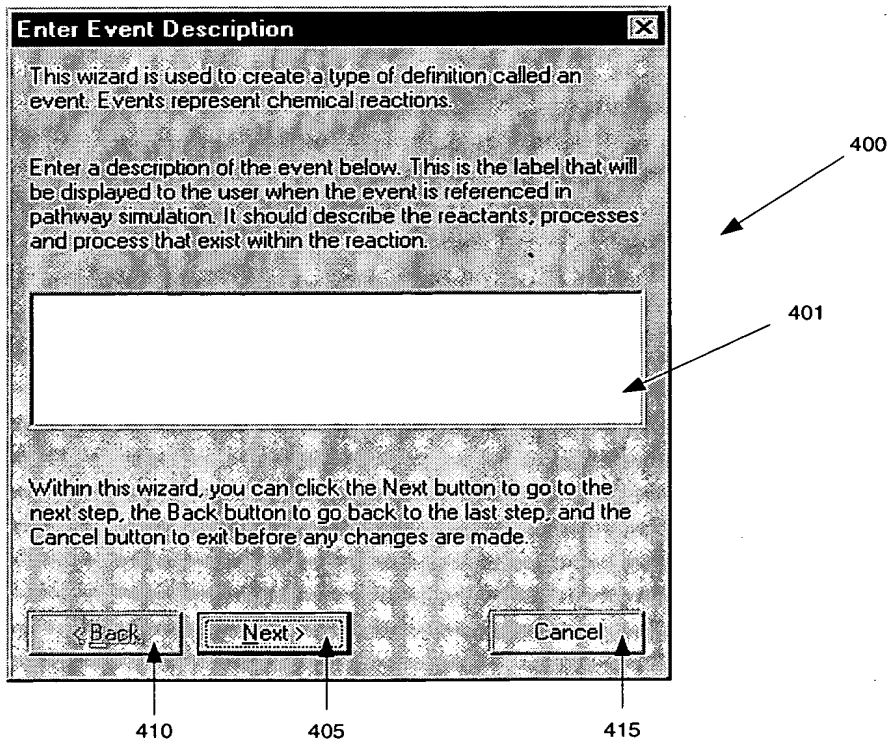


FIGURE 6B

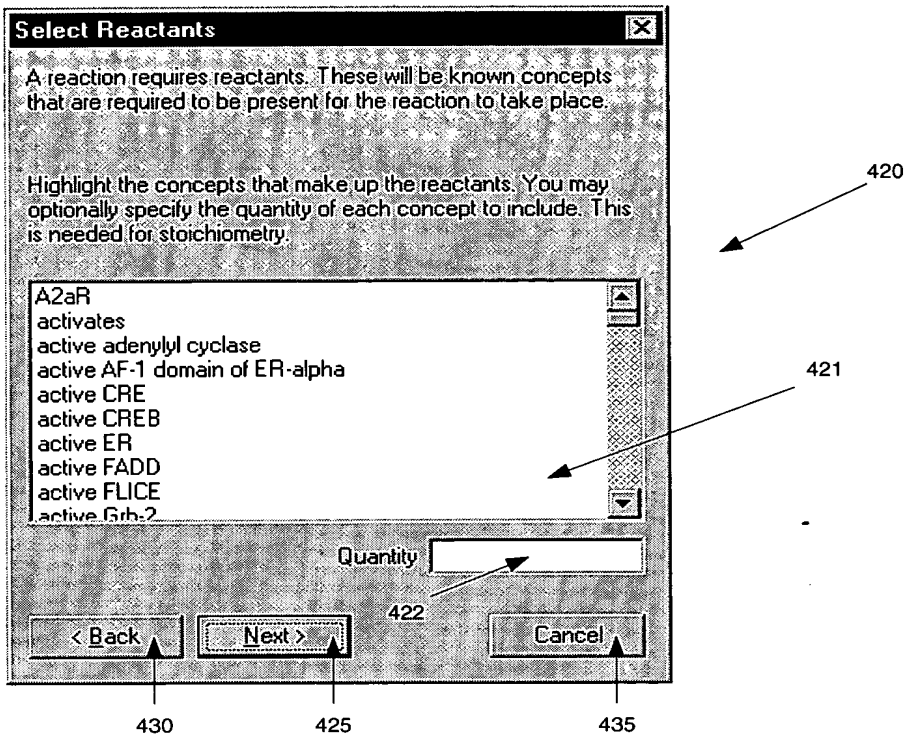


FIGURE 6C

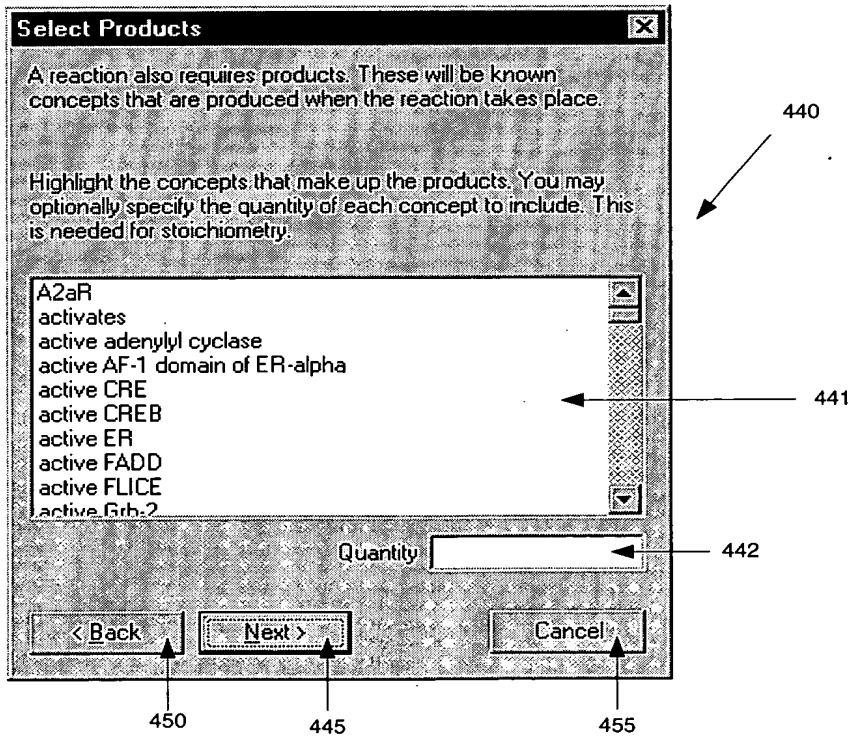


FIGURE 6D

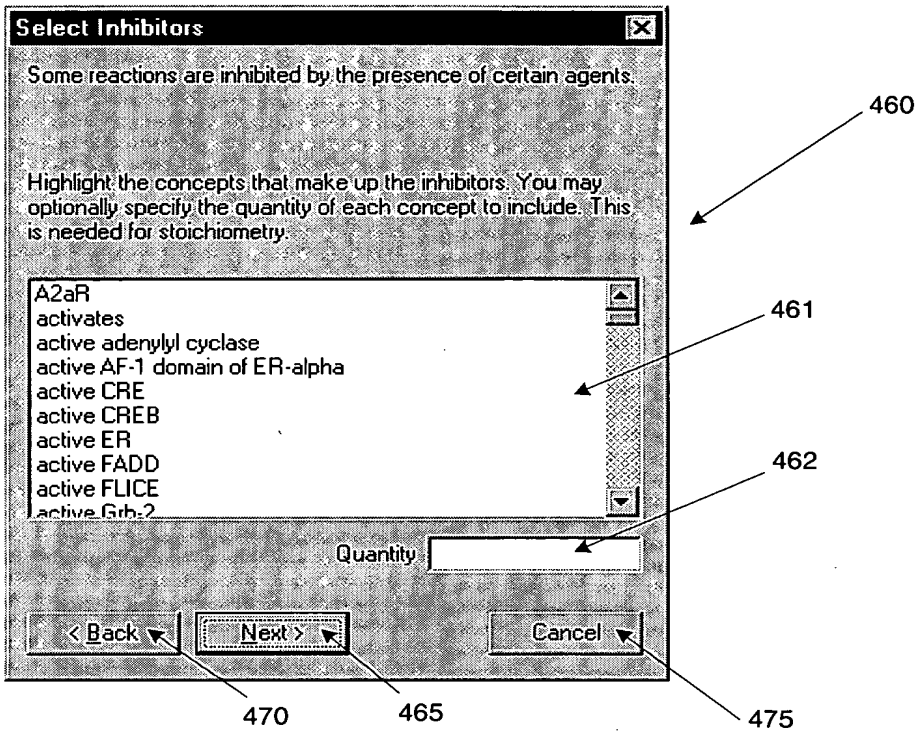


FIGURE 6E

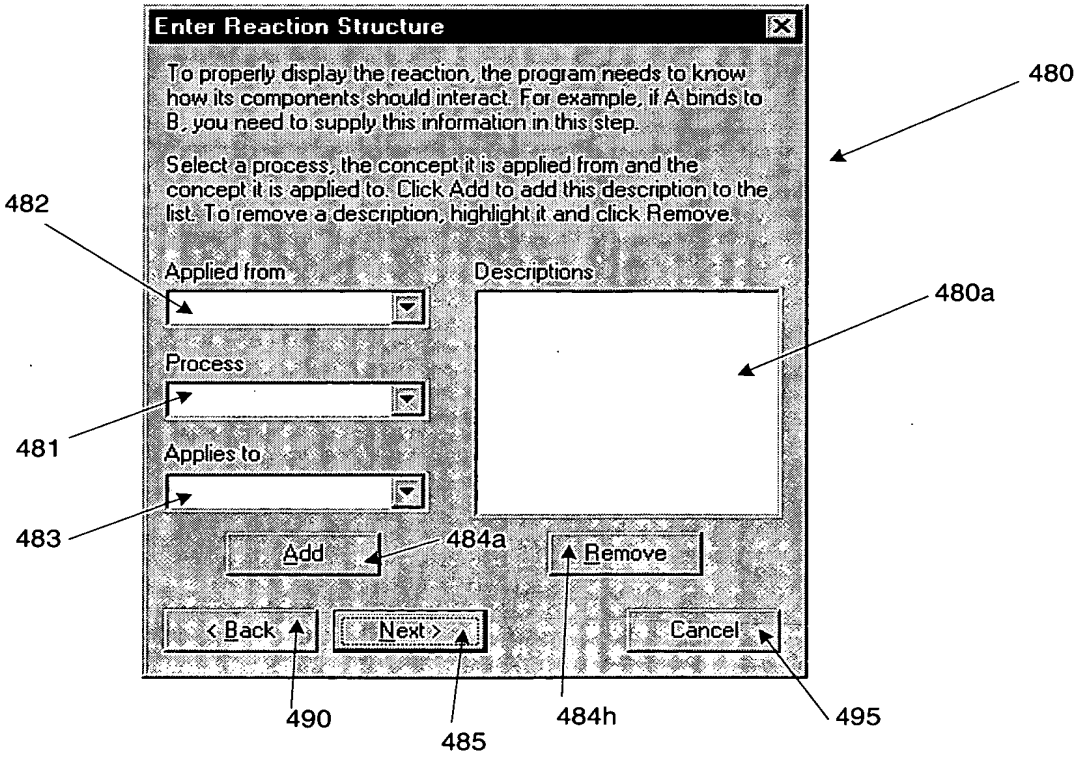


FIGURE 6F

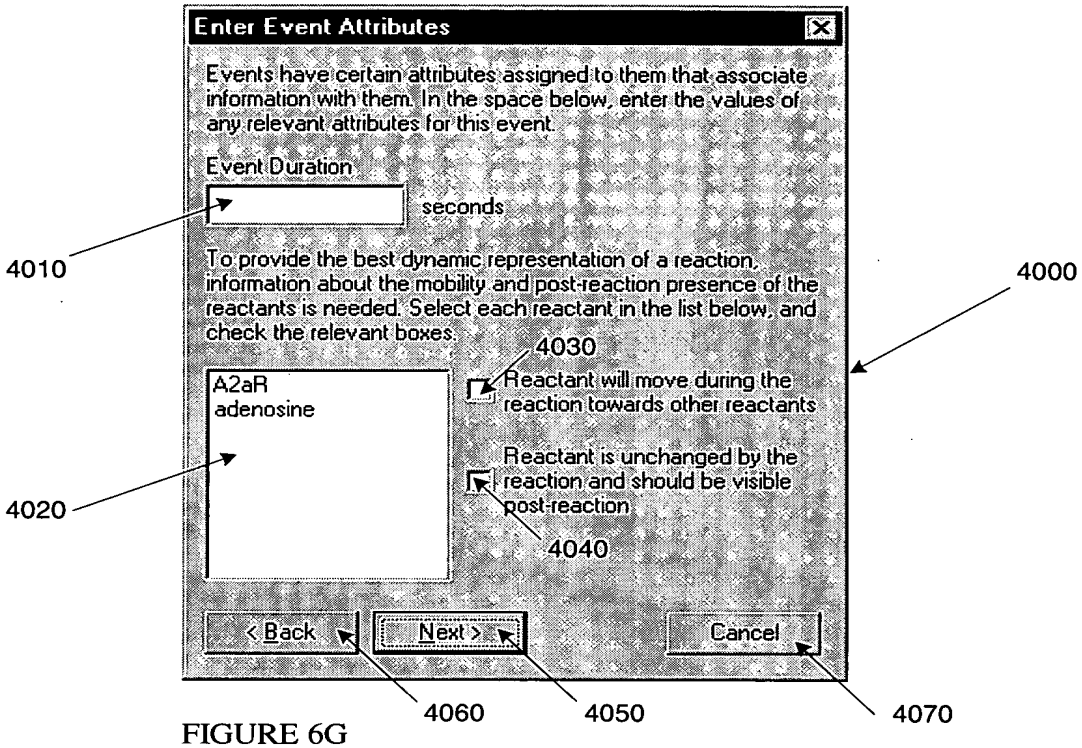


FIGURE 6G

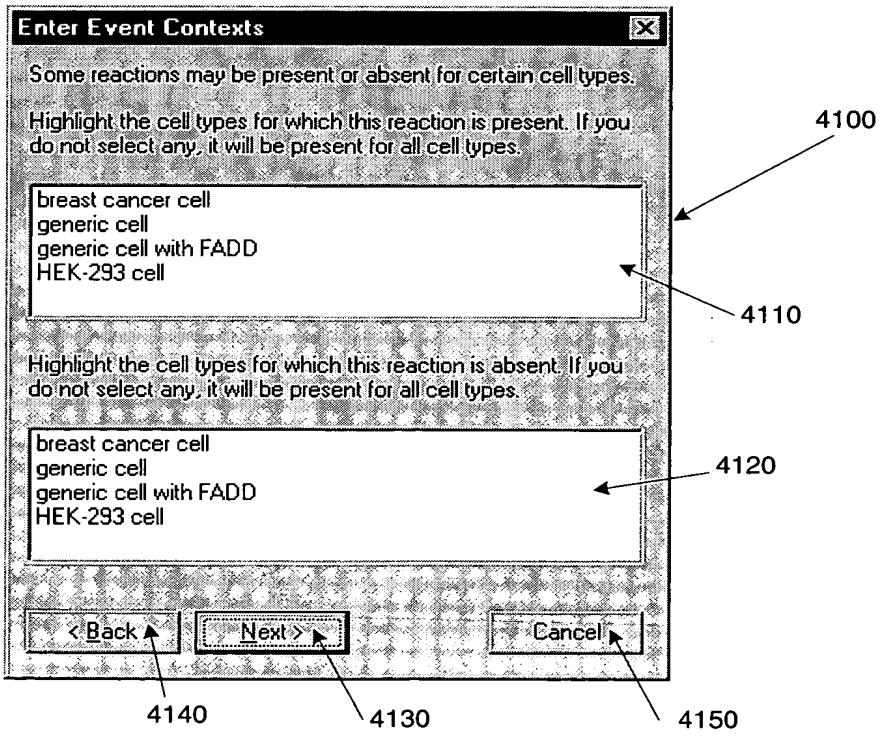


FIGURE 6H

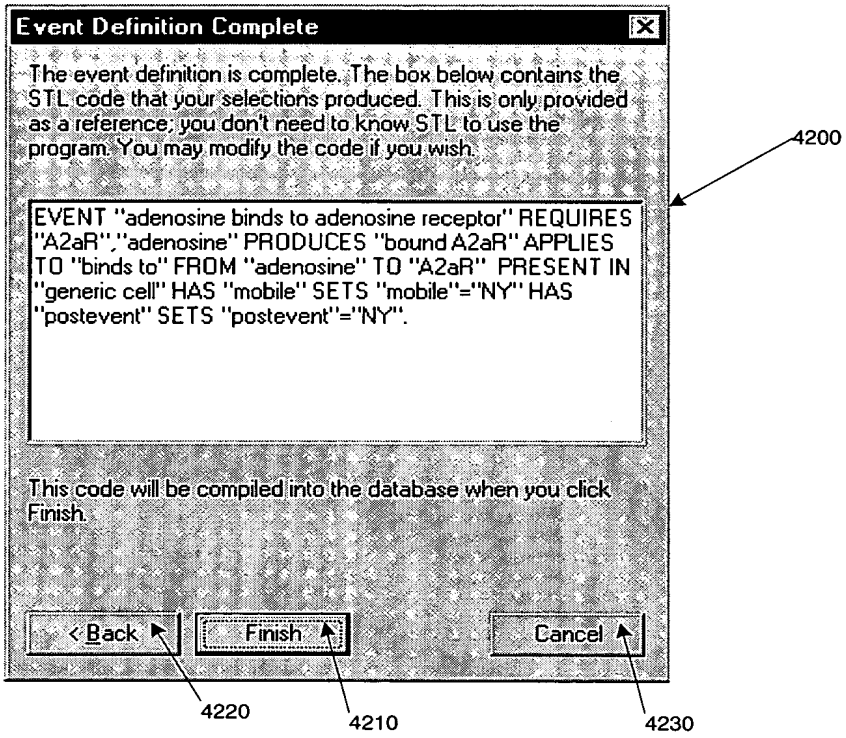


FIGURE 7

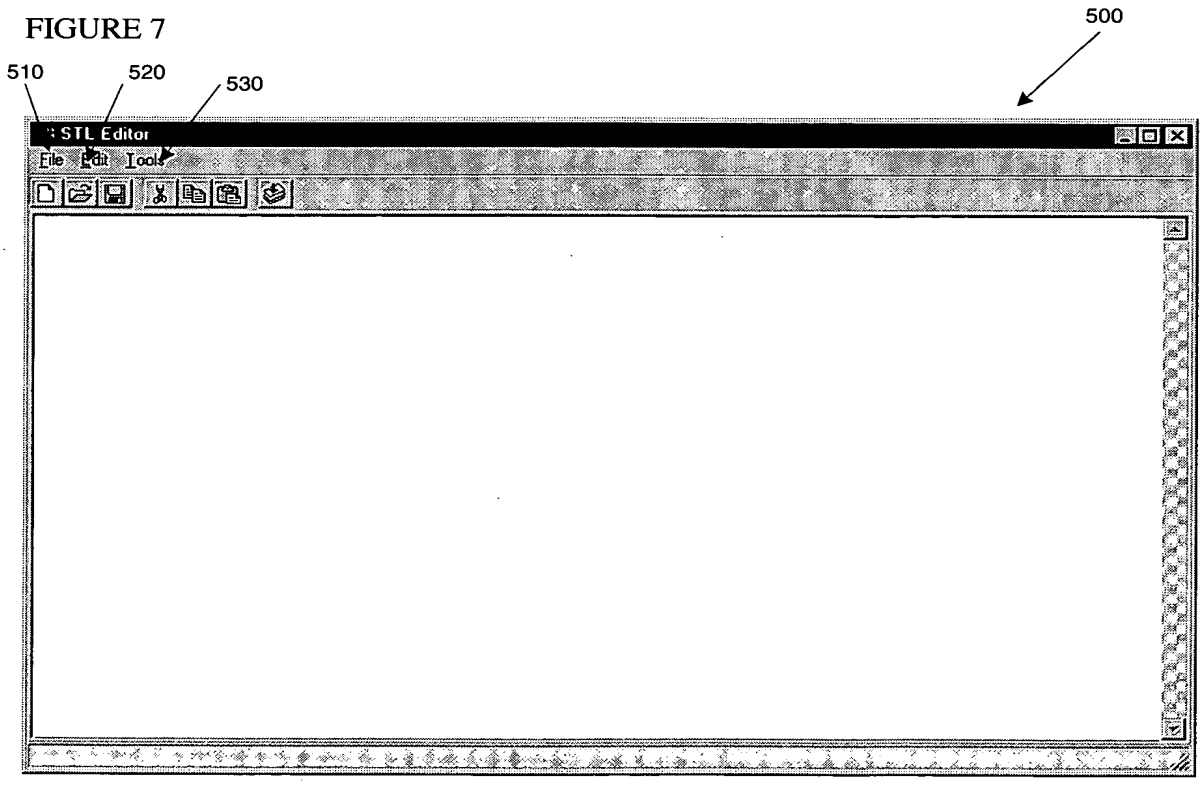


FIGURE 8A

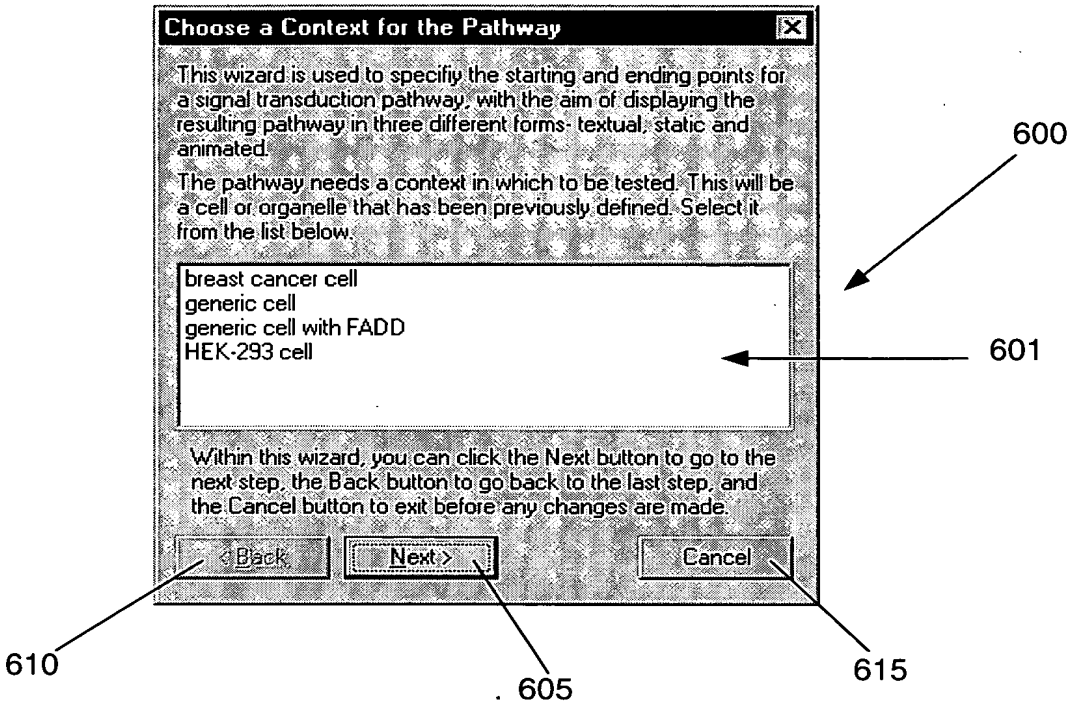


FIGURE 8B

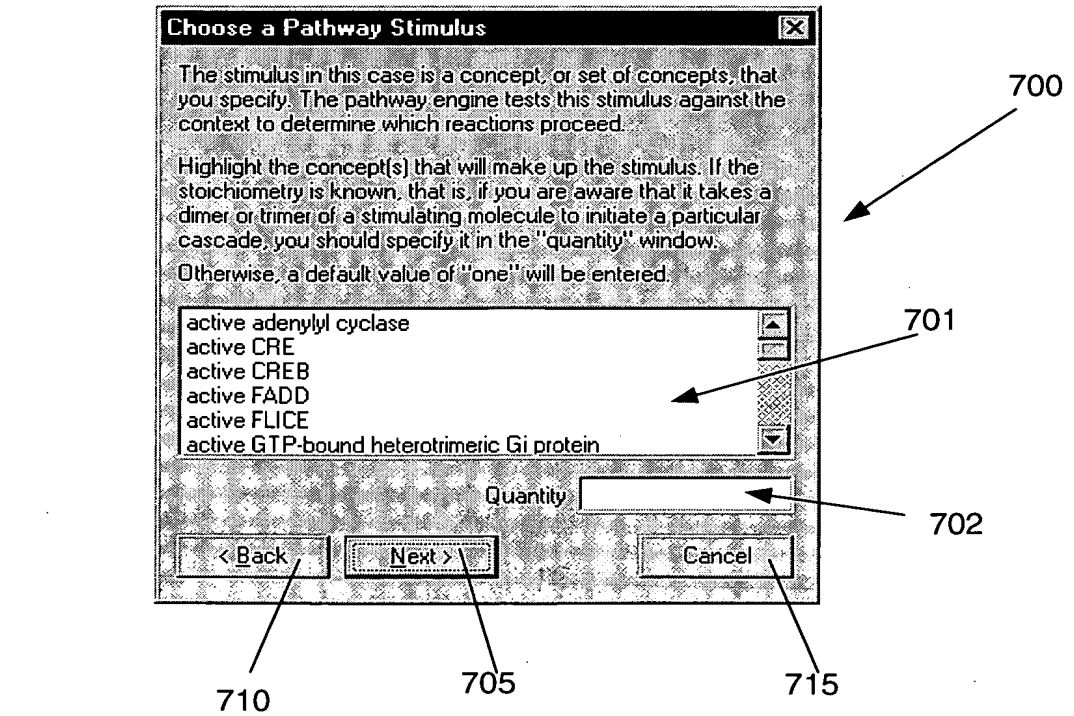


FIGURE 8C

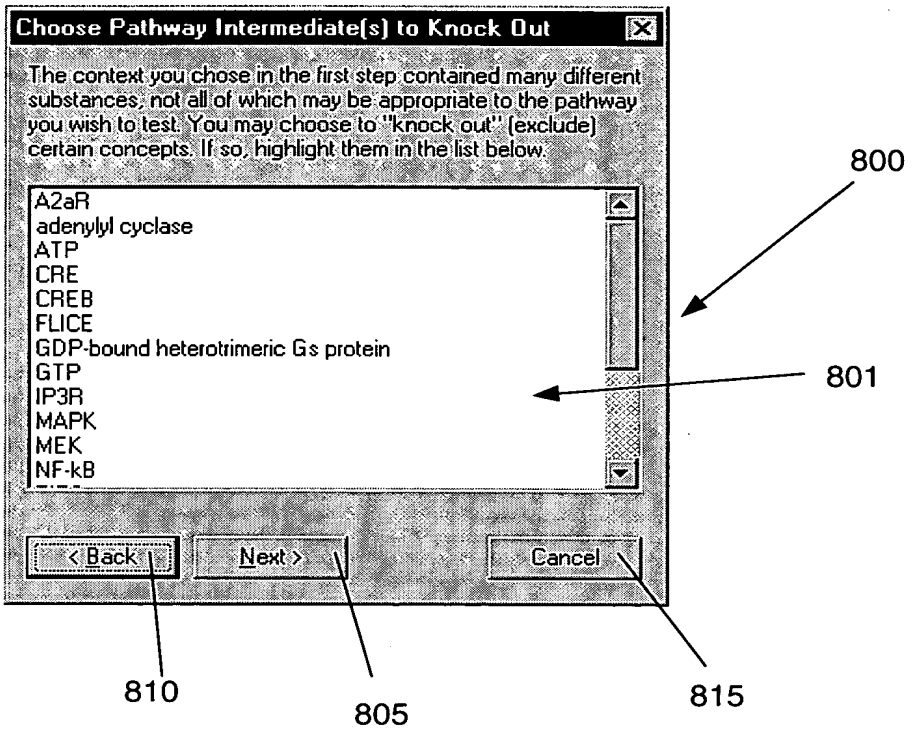


FIGURE 8D

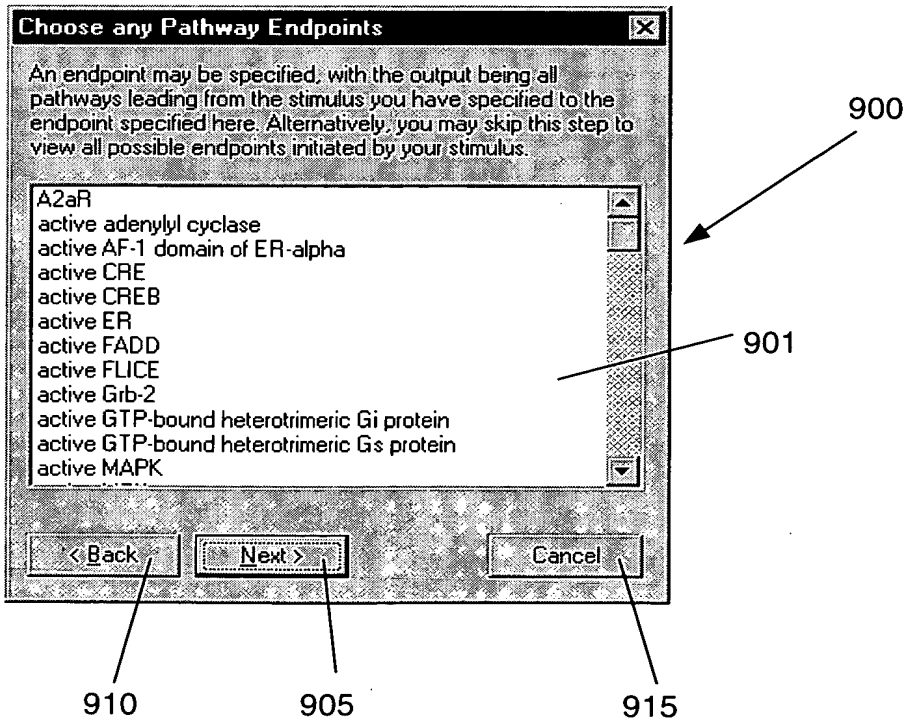


FIGURE 8E

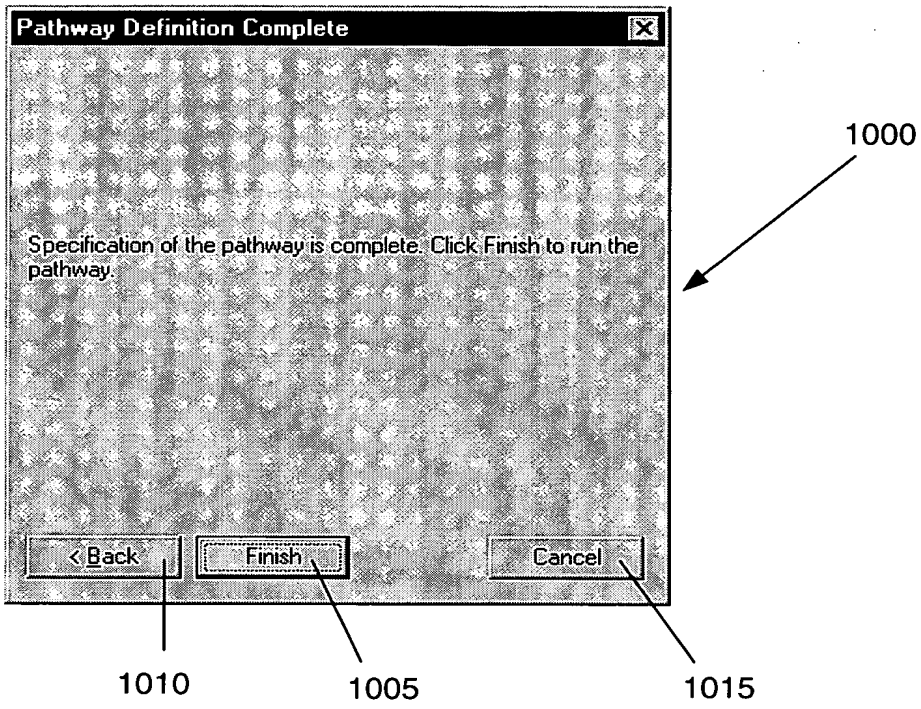


FIGURE 9

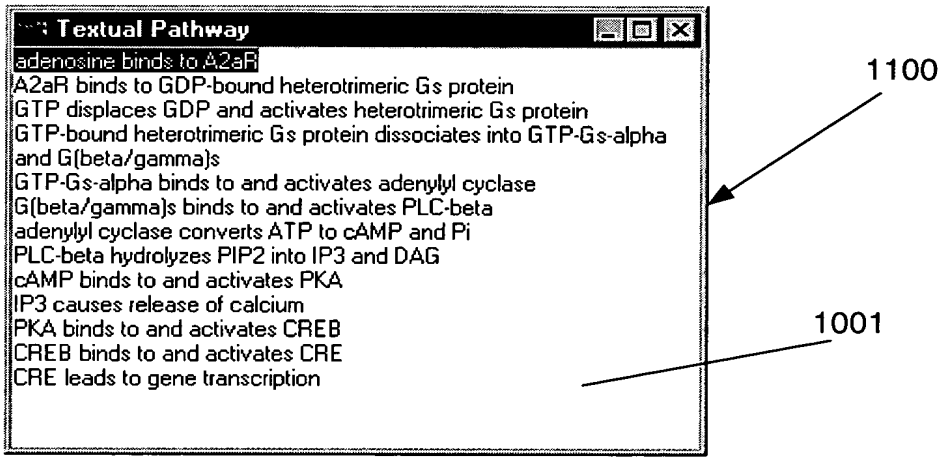


FIGURE 10A

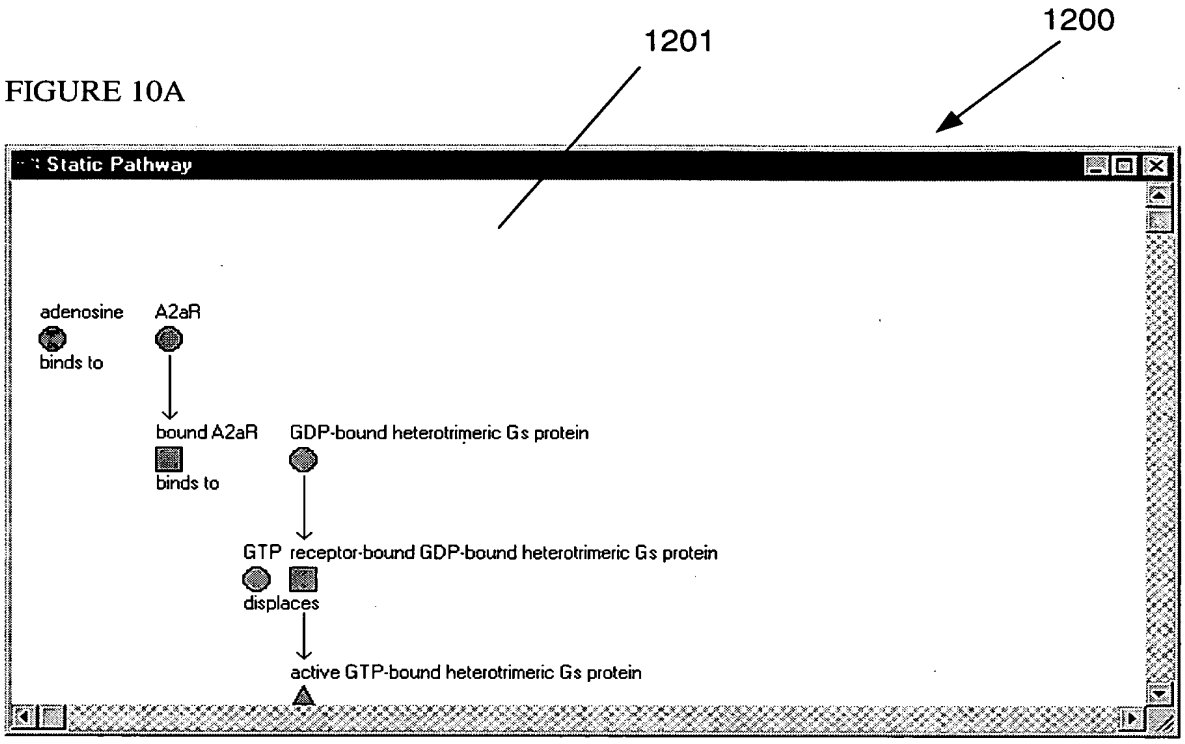


FIGURE 10B

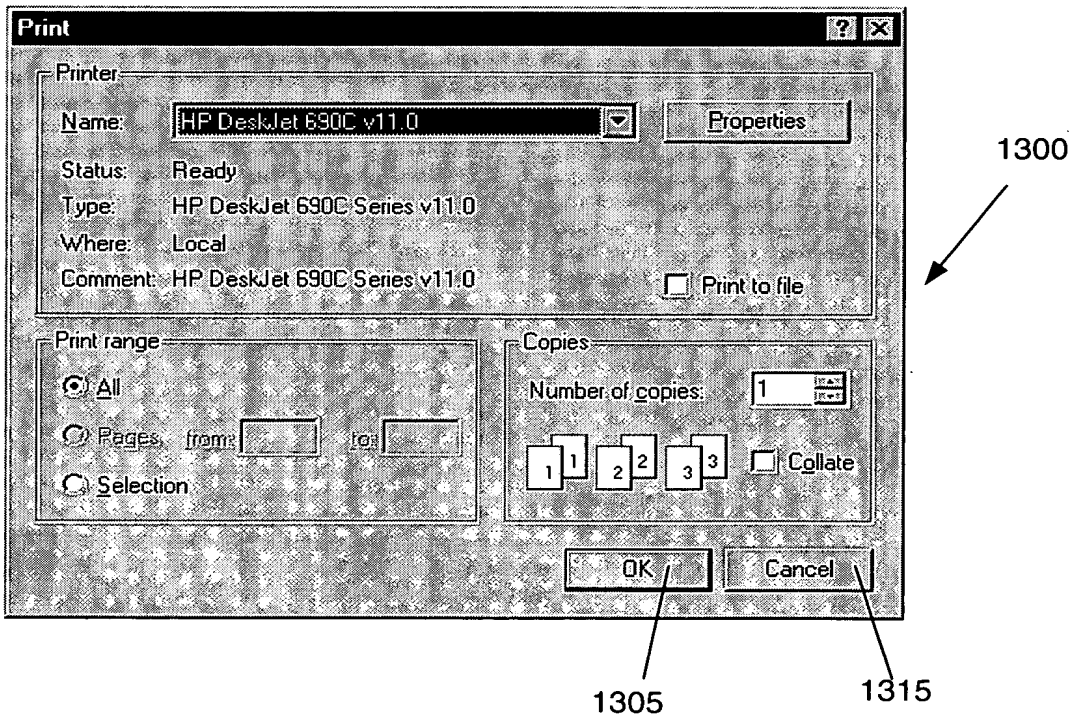


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FIGURE 11

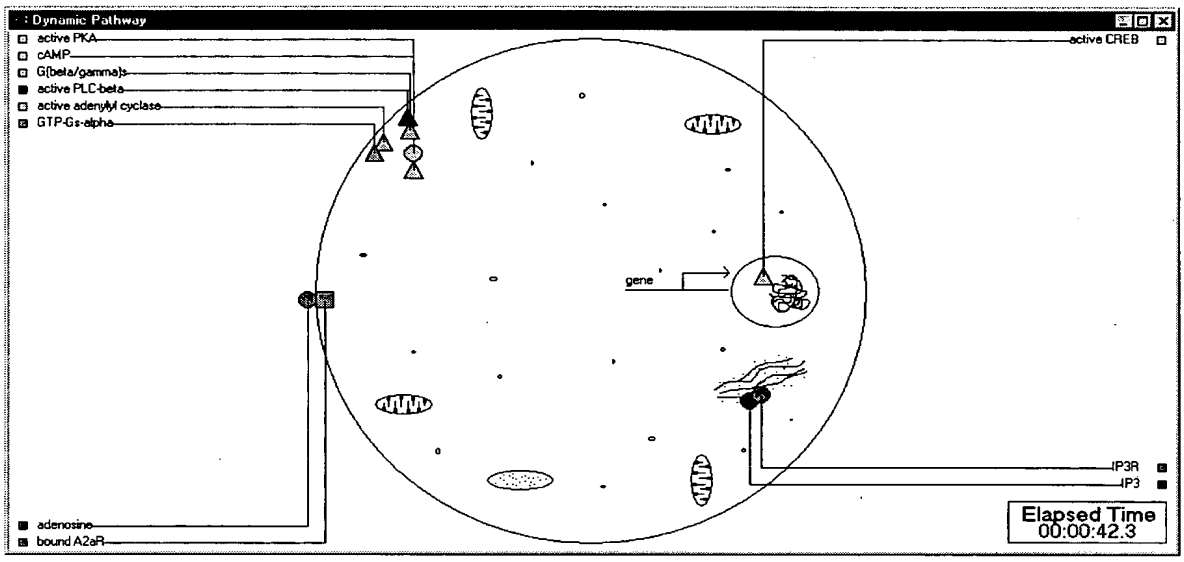
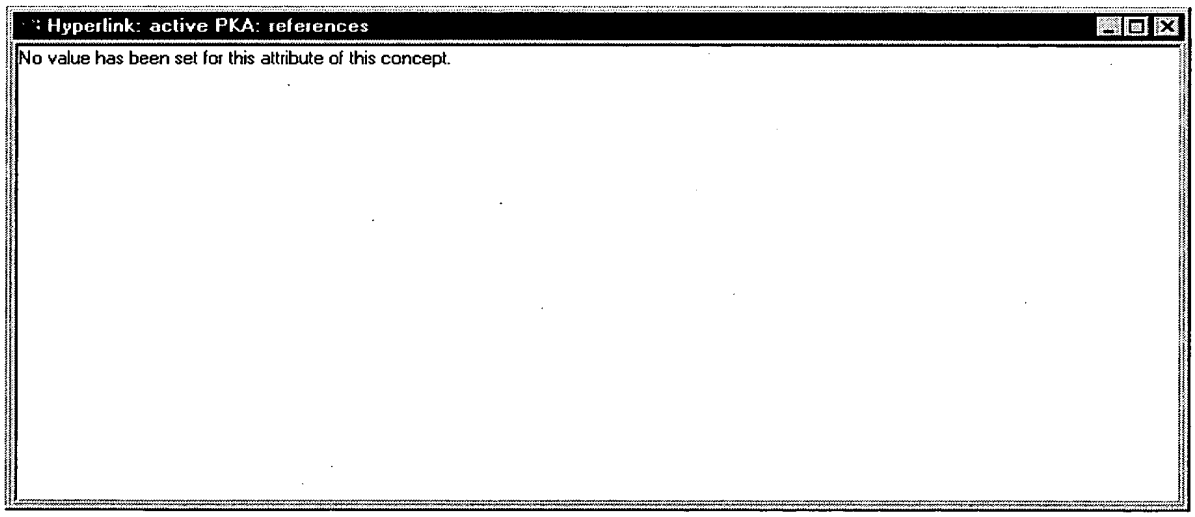


FIGURE 12



1500

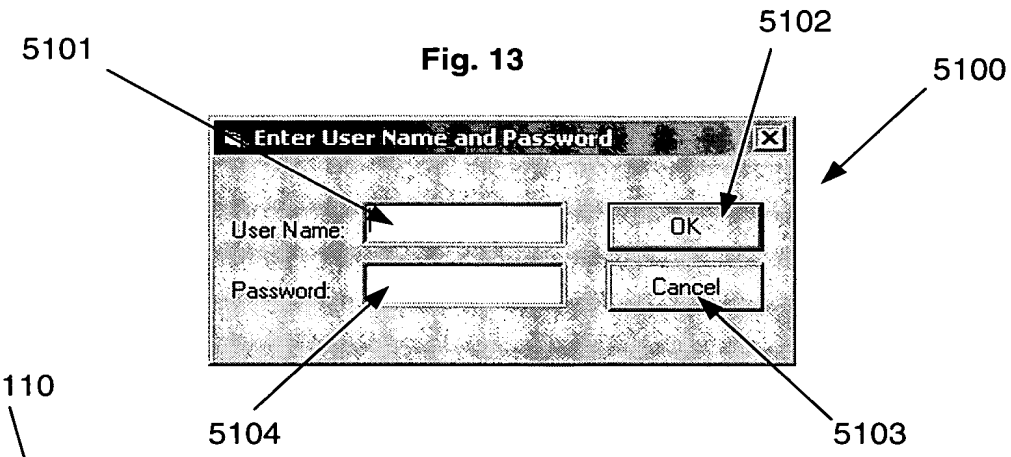

5101
5102
5100
Enter User Name and Password
User Name:
Password:
OK
Cancel
5104
5103

Fig. 13

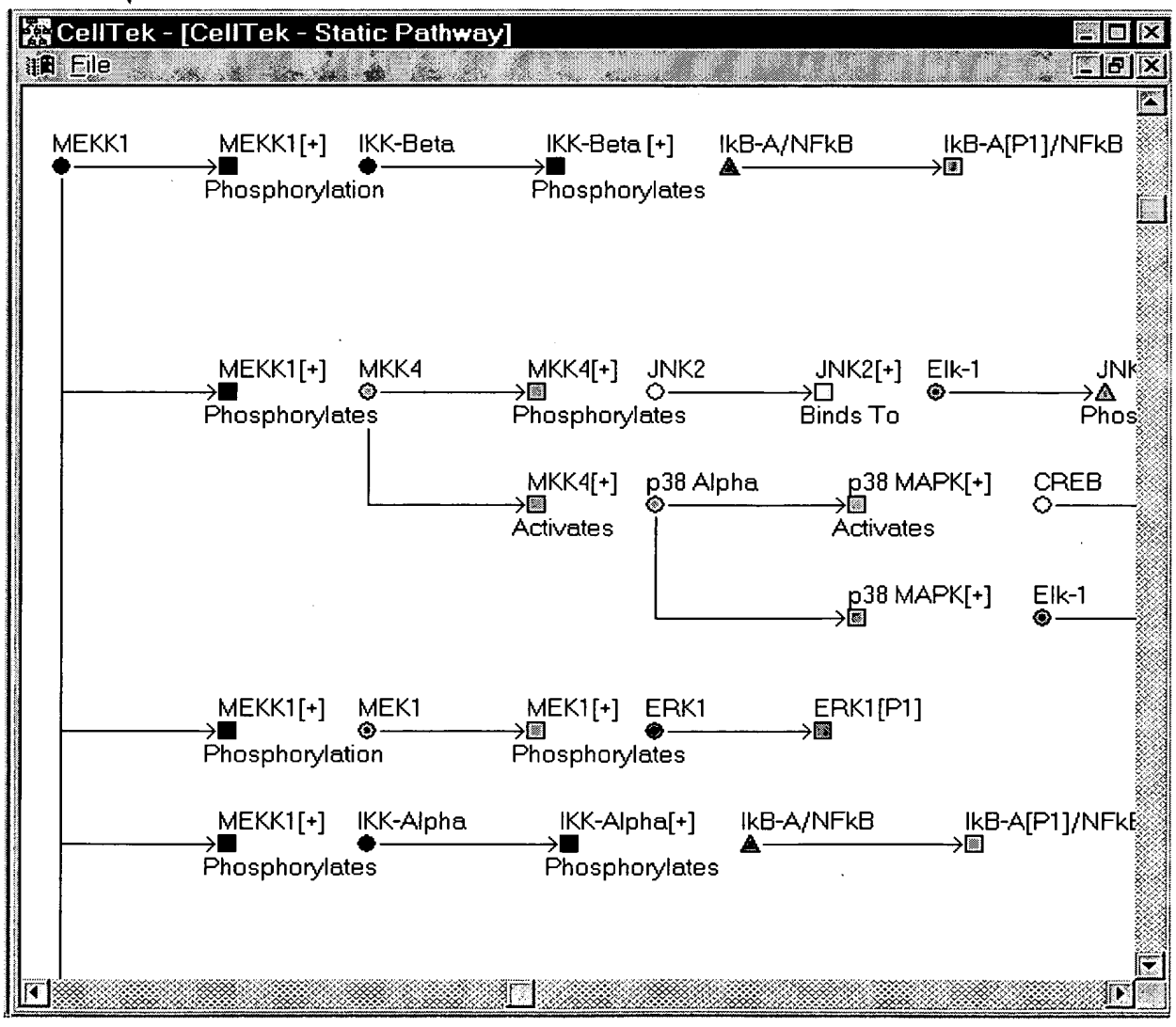
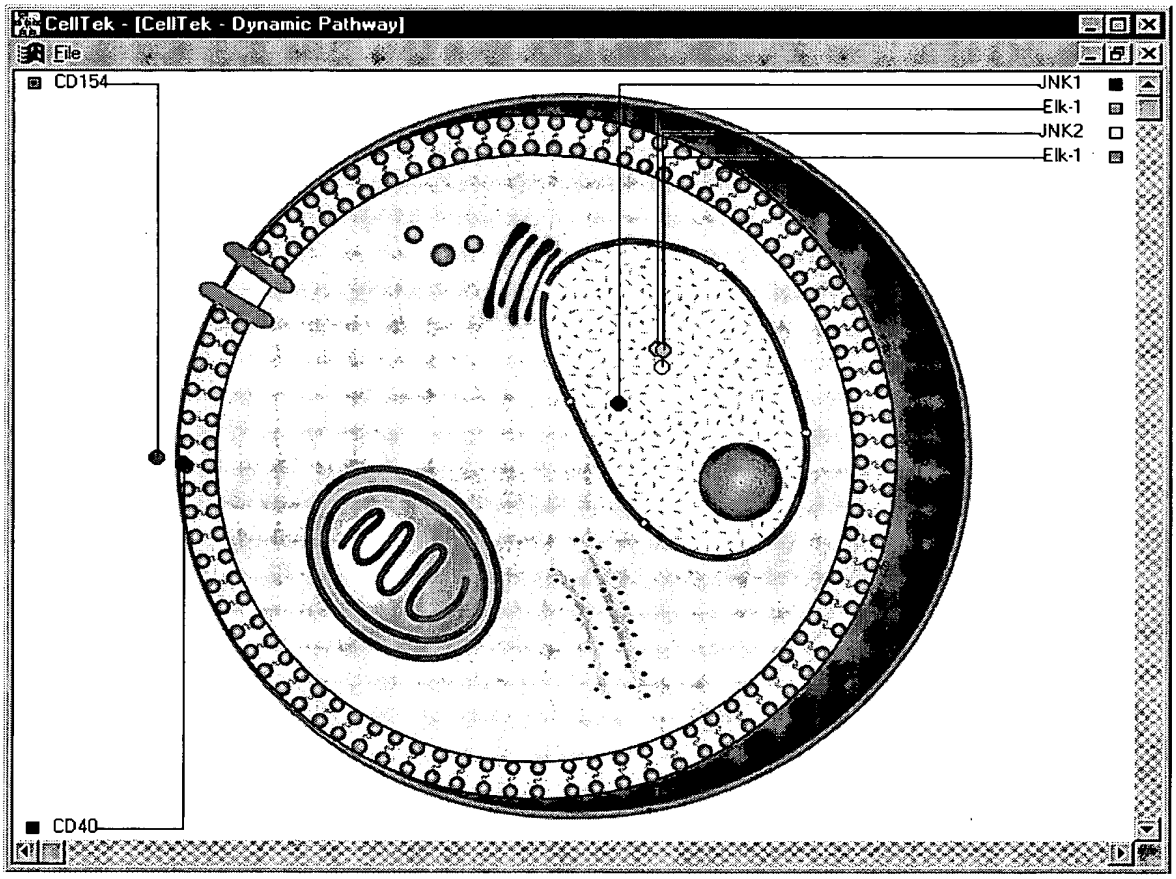

5110
CellTek - [CellTek - Static Pathway]
File
MEKK1
MEKK1[+]
Phosphorylation
IKK-Beta
IKK-Beta [+]
Phosphorylates
IkB-A/NFkB
IkB-A[P1]/NFkB
MEKK1[+]
Phosphorylates
MKK4
MKK4[+]
Phosphorylates
JNK2
JNK2[+]
Binds To
Elk-1
MKK4[+]
Activates
p38 Alpha
p38 MAPK[+]
Activates
CREB
p38 MAPK[+]
Elk-1
MEKK1[+]
Phosphorylation
MEK1
MEK1[+]
Phosphorylates
ERK1
ERK1[P1]
MEKK1[+]
Phosphorylates
IKK-Alpha
IKK-Alpha[+]
Phosphorylates
IkB-A/NFkB
IkB-A[P1]/NFkB

Fig. 14

5120

Fig. 15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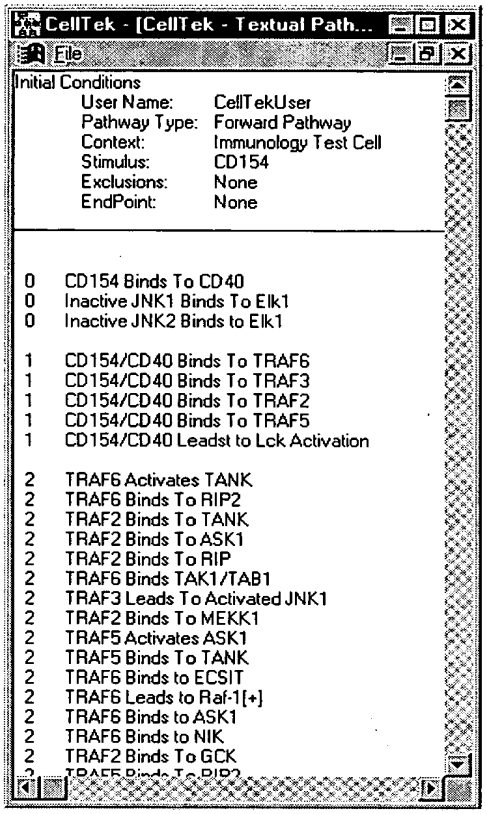
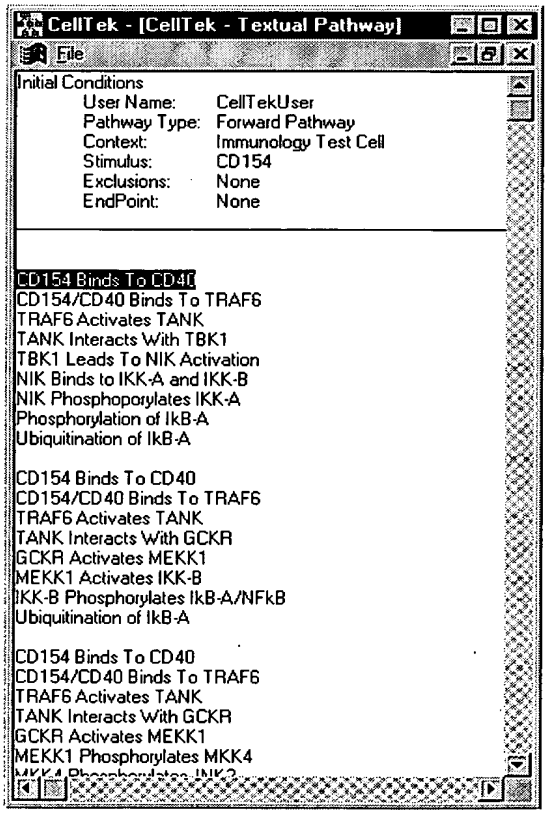
CD154
JNK1
Elk-1
JNK2
Elk-1
CD40

Fig. 16



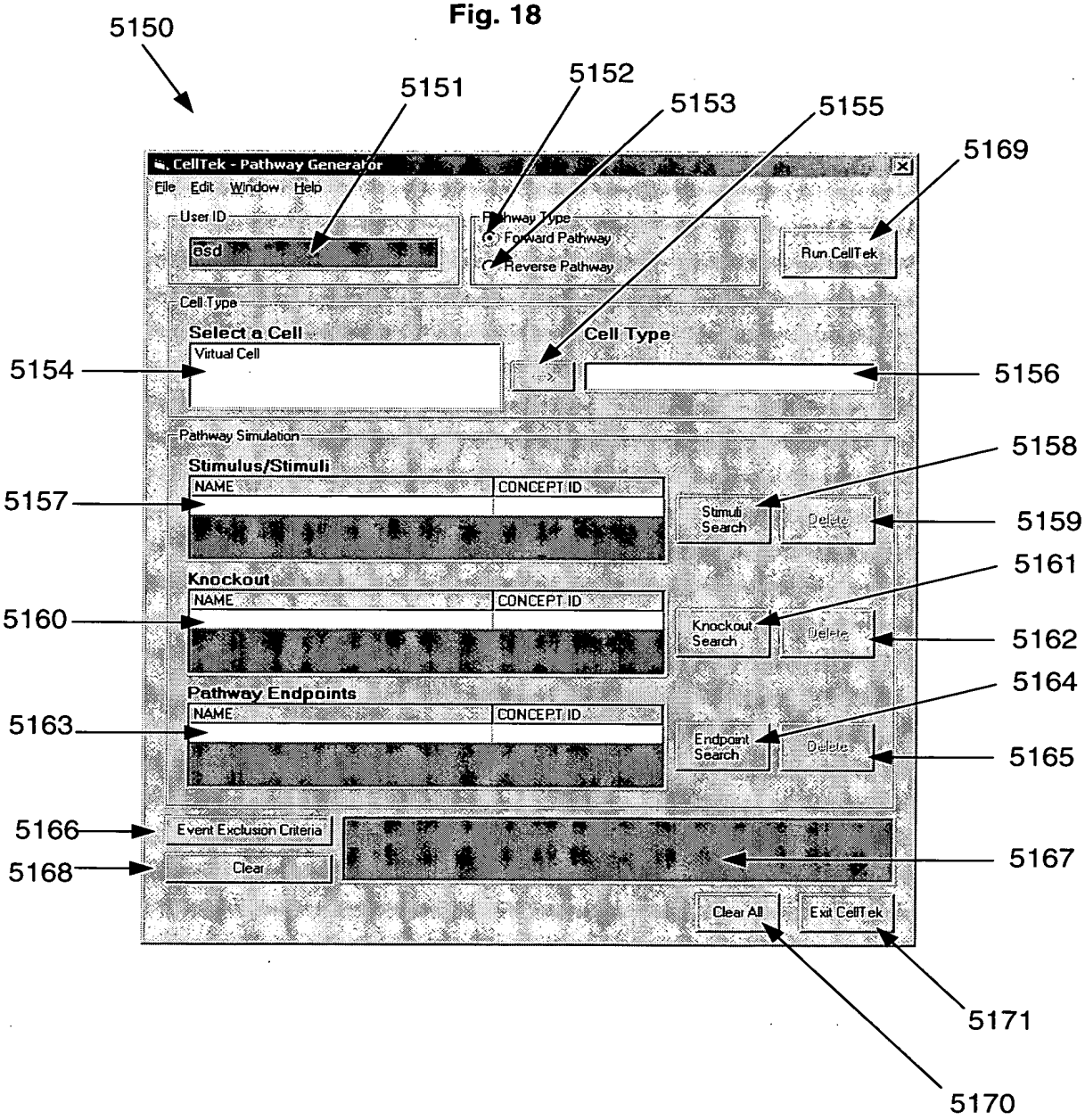
5140

Fig. 17



5130

Fig. 18


5150
5151
5152
5153
5155
5169
CellTek - Pathway Generator
File Edit Window Help
User ID
osd
Pathway Type
Forward Pathway
Reverse Pathway
Run CellTek
Cell Type
Select a Cell
Virtual Cell
Cell Type
5154
5156
Pathway Simulation
Stimulus/Stimuli
NAME
CONCEPT ID
5157
5158
Stimuli Search
Delete
5159
Knockout
NAME
CONCEPT ID
5160
5161
Knockout Search
Delete
5162
Pathway Endpoints
NAME
CONCEPT ID
5163
5164
Endpoint Search
Delete
5165
5166
Event Exclusion Criteria
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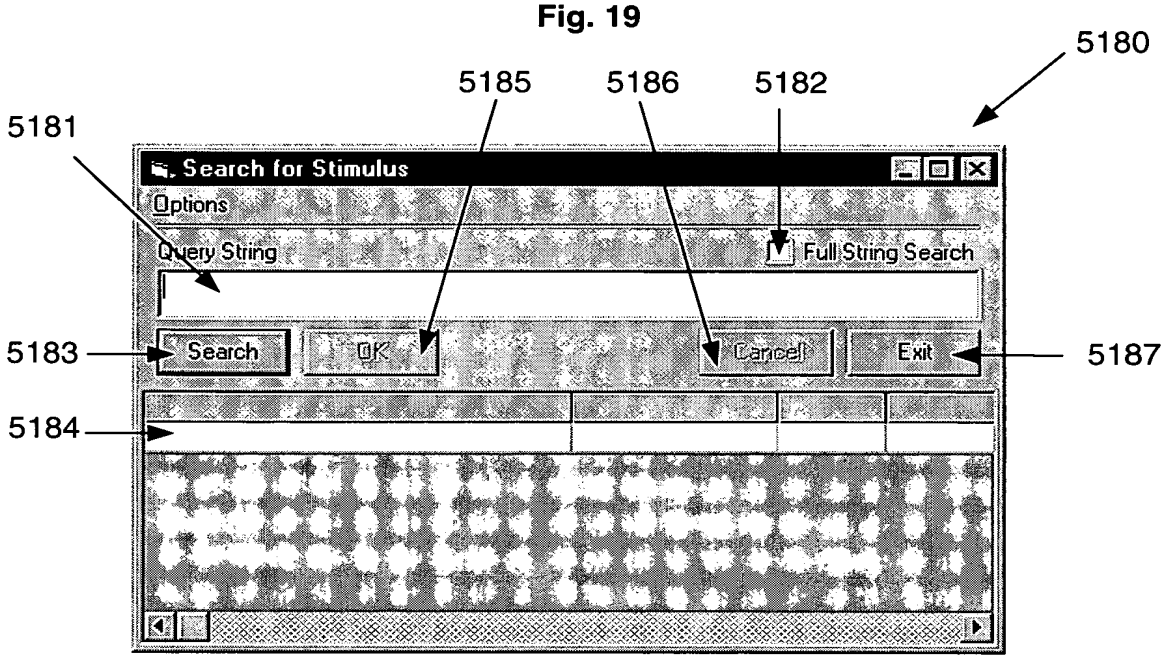
Clear
5167
Clear All
Exit CellTek
5171
5170

Fig. 19


5180
5185
5186
5182
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Search for Stimulus
Options
Query String
Full String Search
5183
Search
OK
Cancel
Exit
5187
5184

Fig. 20

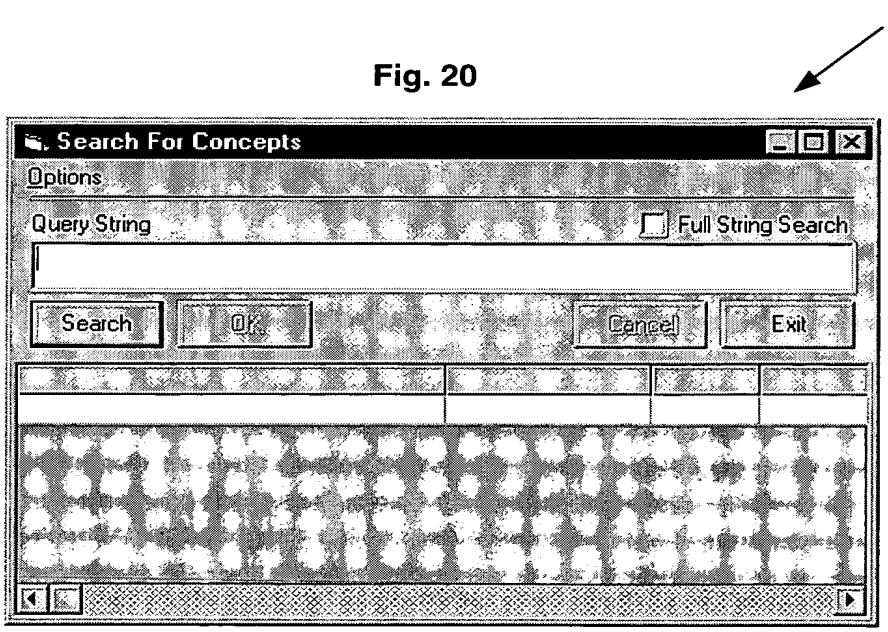

5190
Search For Concepts
Options
Query String
Full String Search
Search
OK
Cancel
Exit

Fig. 21

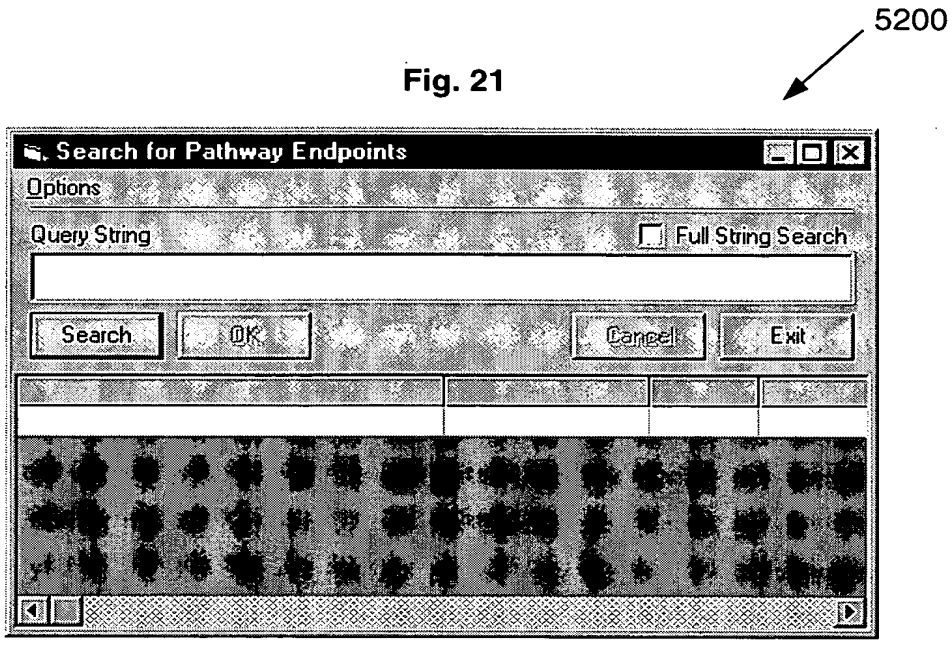


Fig. 22

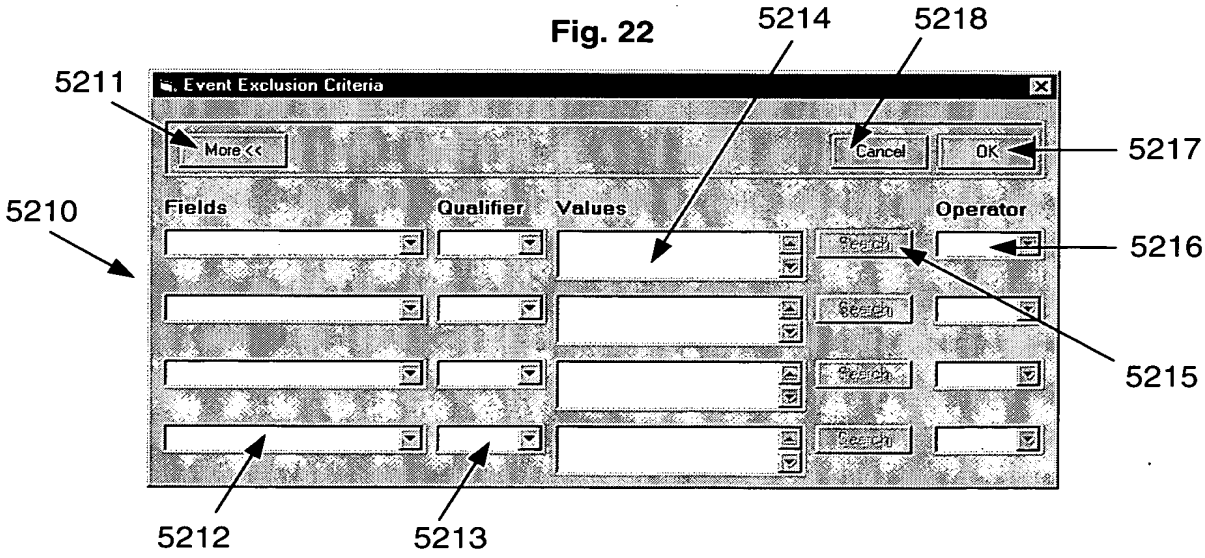


Fig. 23

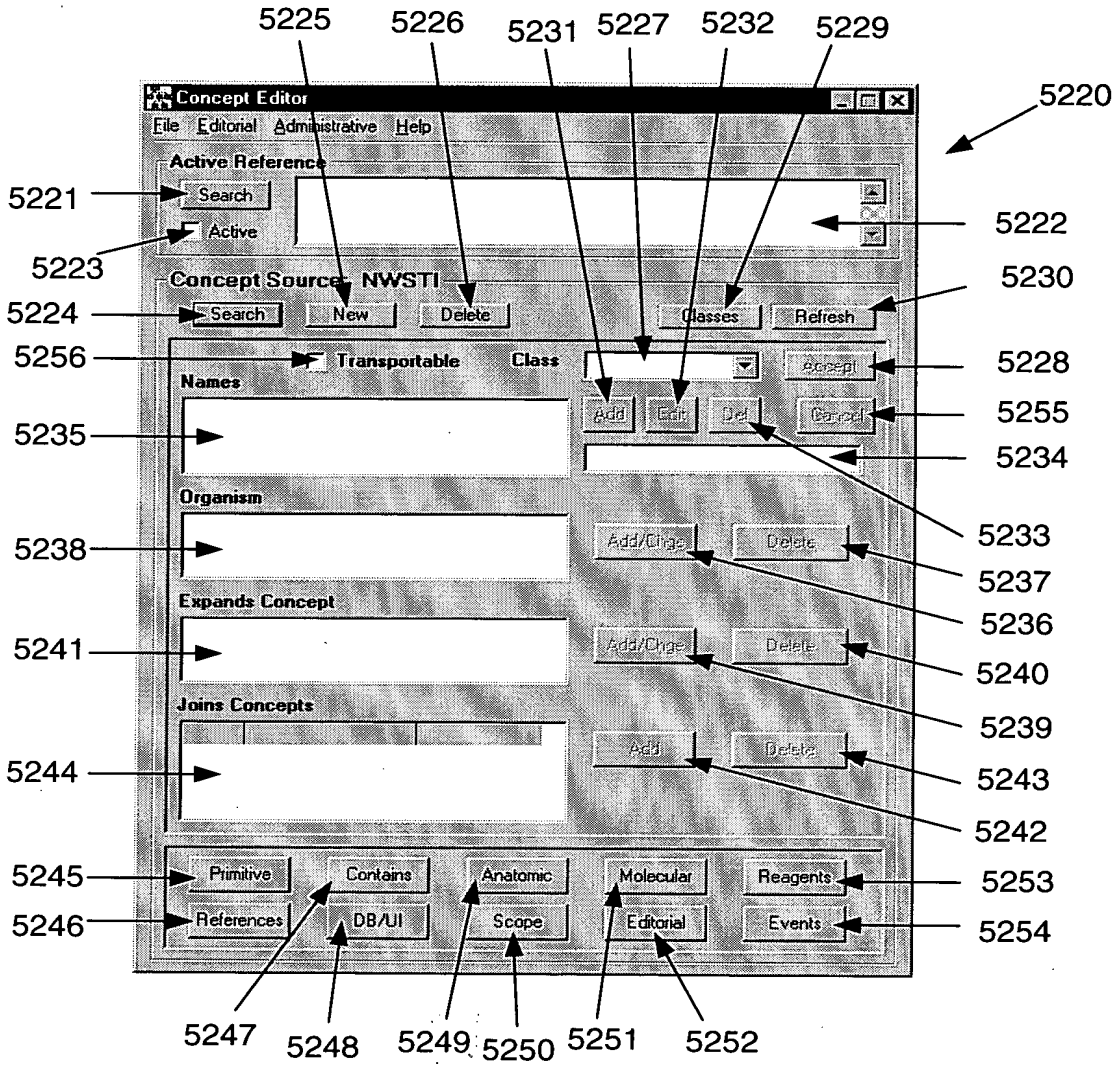

5225
5226
5231
5227
5232
5229
5220
Concept Editor
File Editorial Administrative Help
Active Reference
5221
Search
Active
5223
5222
Concept Source: NWSTI
5230
5224
Search
New
Delete
Classes
Refresh
5256
Transportable
Class
Accept
5228
Names
Add
Edit
Del
Cancel
5255
5235
5234
Organism
5238
Add/Chge
Delete
5233
5237
5236
Expands Concept
5241
Add/Chge
Delete
5240
5239
Joins Concepts
5244
Add
Delete
5243
5242
5245
Primitive
Contains
Anatomic
Molecular
Reagents
5253
5246
References
DB/UI
Scope
Editorial
Events
5254
5247
5248
5249
5250
5251
5252

Fig. 24

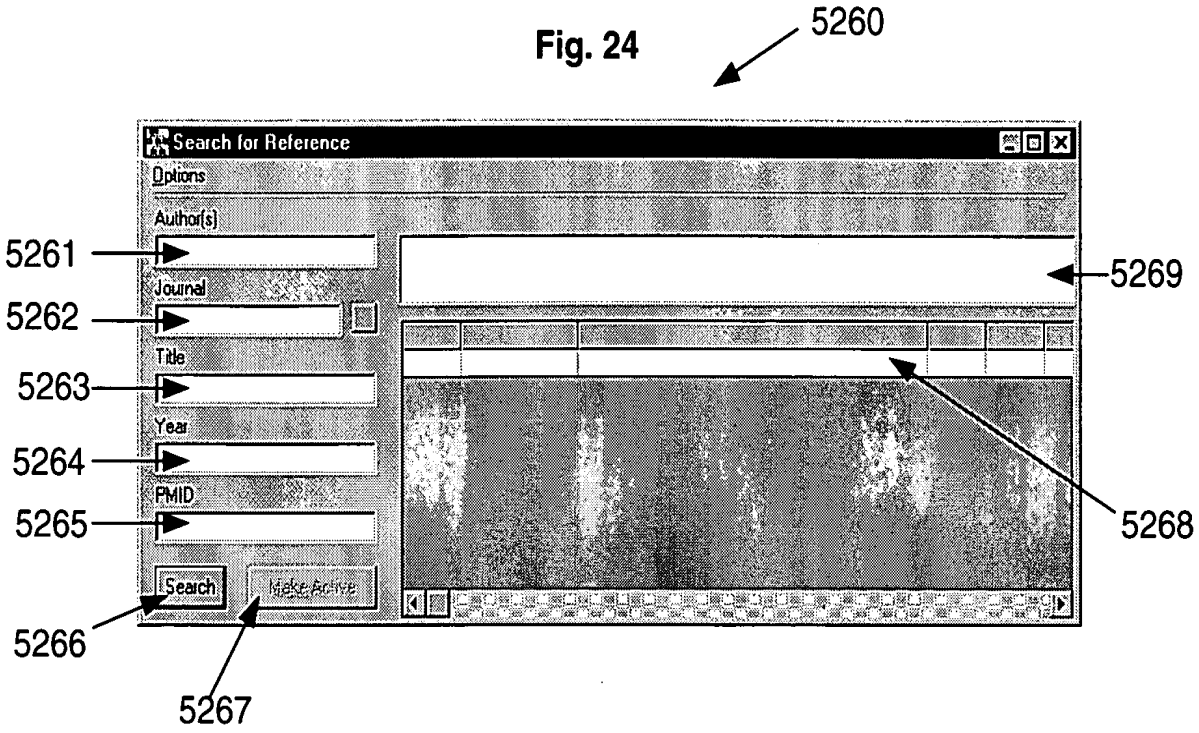

5260
Search for Reference
Options
Author(s)
Journal
Title
Year
PMID
Search
Make Active
5261
5262
5263
5264
5265
5266
5267
5268
5269

Fig. 25

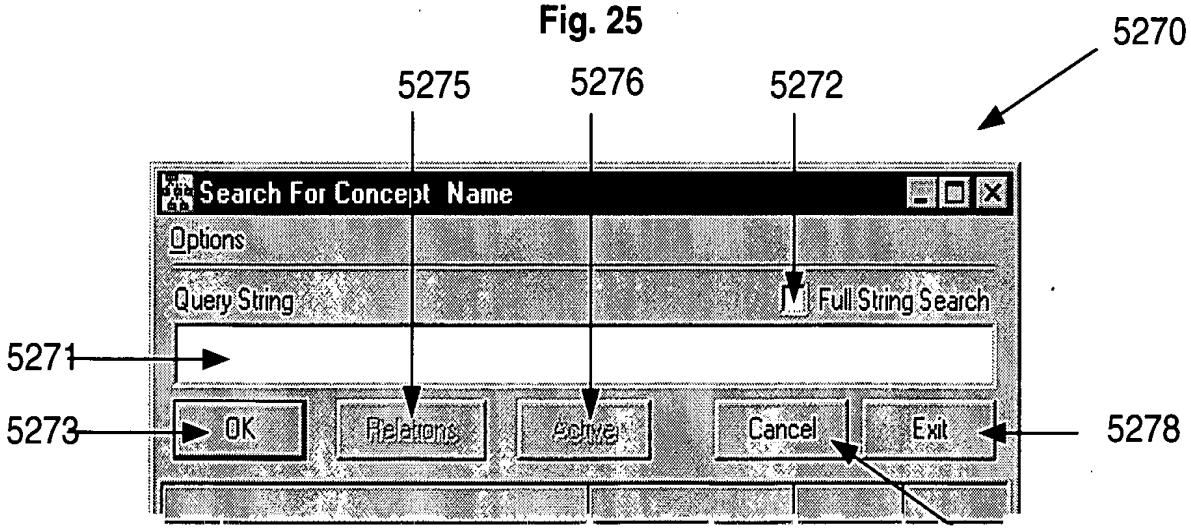

5270
5275
5276
5272
Search For Concept Name
Options
Query String
Full String Search
5271
5273
OK
Relations
Active
Cancel
Exit
5278

Fig. 26

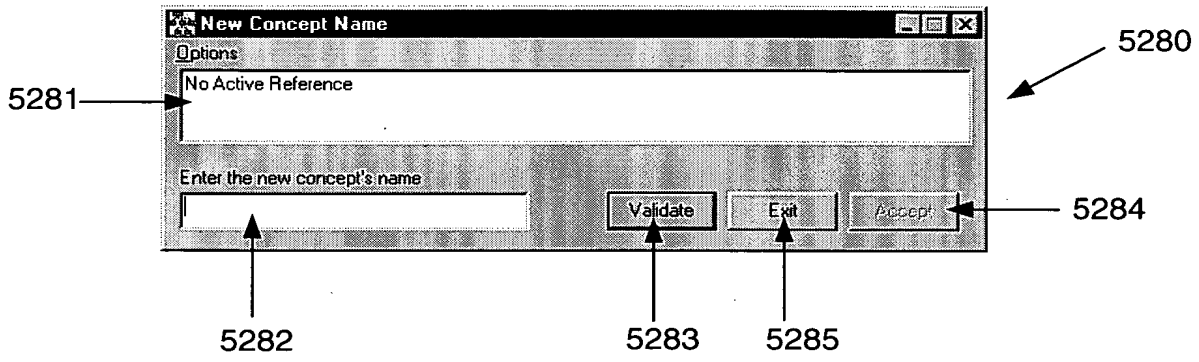

New Concept Name
Options
No Active Reference
Enter the new concept's name
Validate
Exit
Accept
5280
5281
5284
5282
5283
5285

Fig. 27

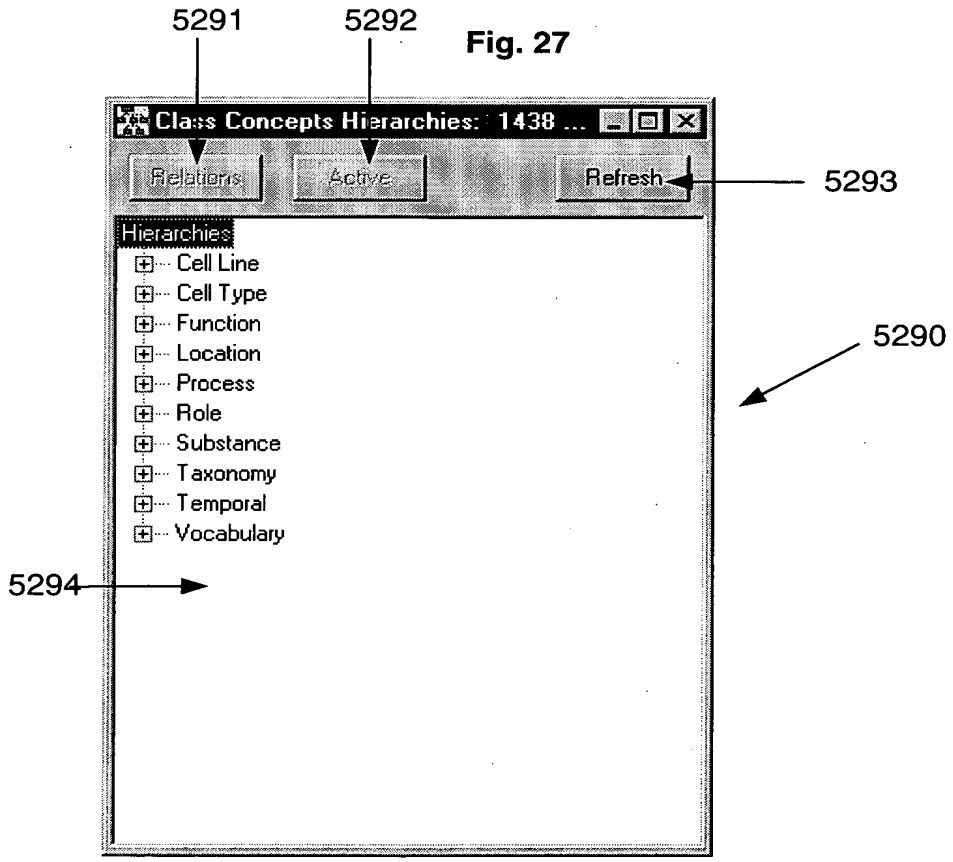

5291
5292
Class Concepts Hierarchies: 1438 ...
Relations
Active
Refresh
5293
Hierarchies
Cell Line
Cell Type
Function
Location
Process
Role
Substance
Taxonomy
Temporal
Vocabulary
5290
5294

Fig. 28

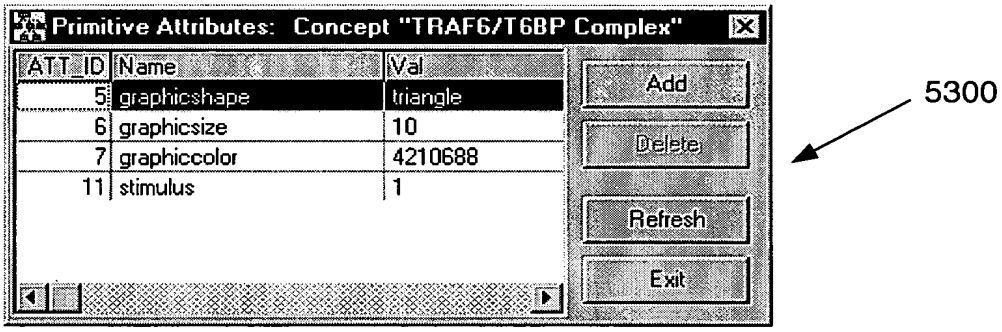

Primitive Attributes: Concept "TRAF6/T6BP Complex"
ATT_ID
Name
Val
5
graphicshape
triangle
6
graphicsize
10
7
graphiccolor
4210688
11
stimulus
1
Add
Delete
Refresh
Exit
5300

Fig. 29

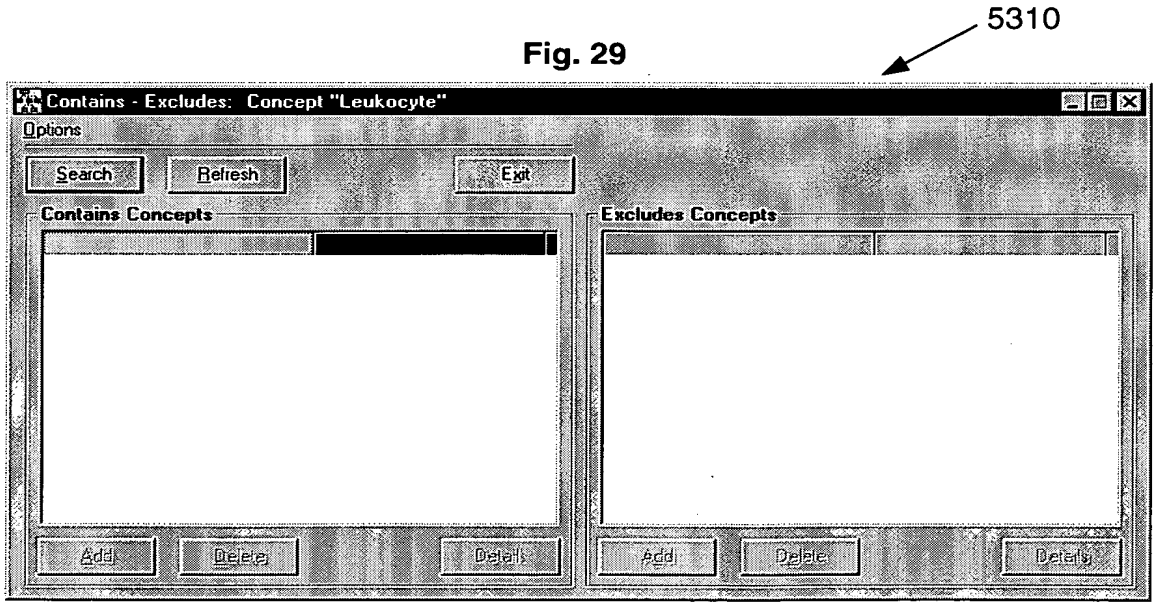
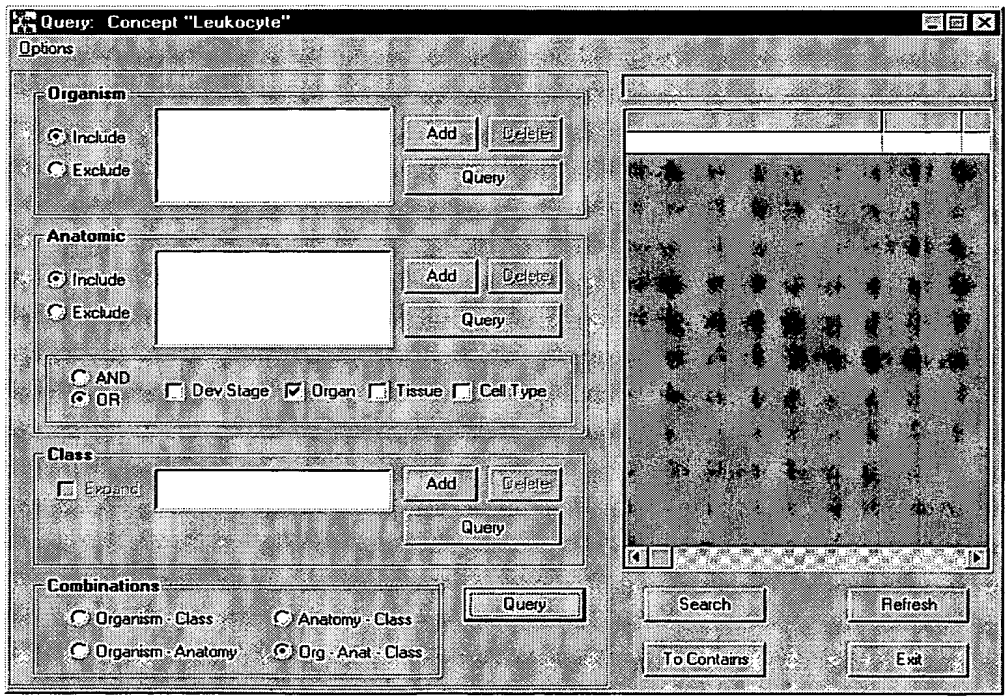
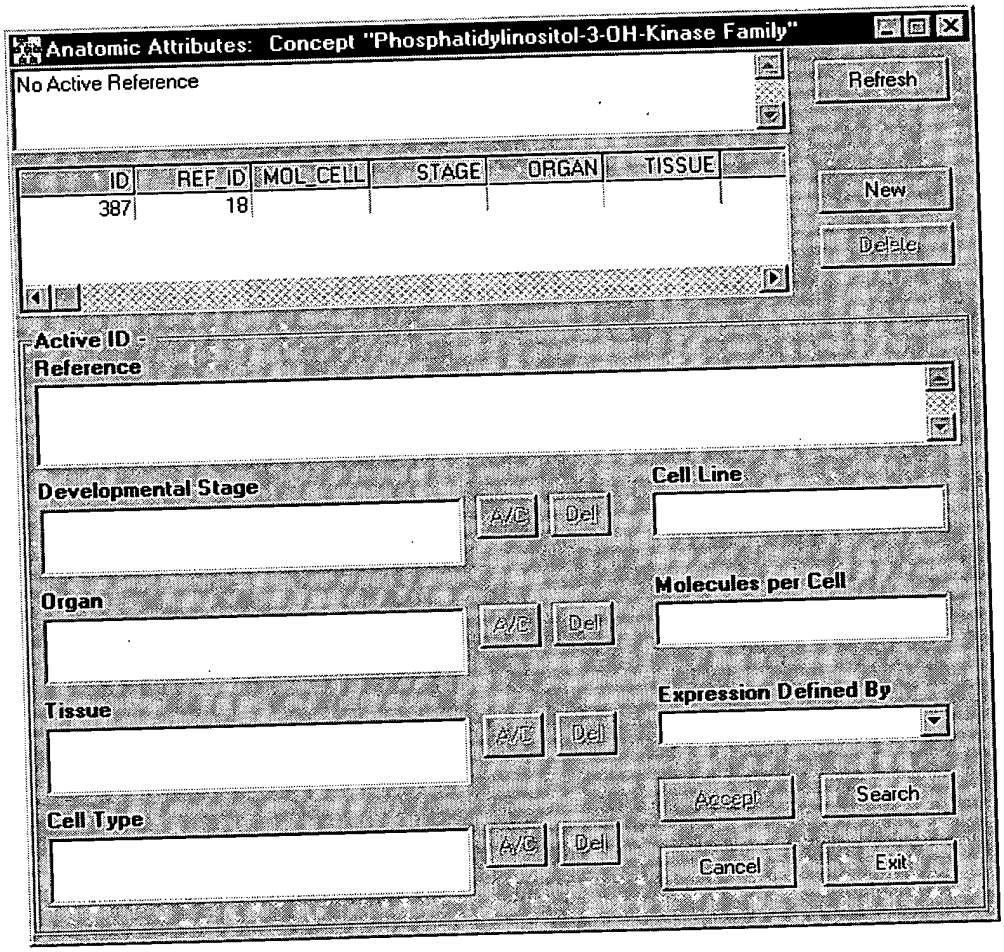

5310
Contains - Excludes: Concept "Leukocyte"
Options
Search
Refresh
Exit
Contains Concepts
Excludes Concepts
Add
Delete
Details
Add
Delete
Details

Fig. 30


Query: Concept "Leukocyte"
Options
Organism
Include
Exclude
Add
Delete
Query
Anatomic
Include
Exclude
Add
Delete
Query
AND
OR
Dev Stage
Organ
Tissue
Cell Type
Class
Expand
Add
Delete
Query
Combinations
Organism - Class
Anatomy - Class
Organism - Anatomy
Org - Anat - Class
Query
Search
Refresh
To Contains
Exit

5320

Fig. 31


Anatomic Attributes: Concept "Phosphatidylinositol-3-OH-Kinase Family"
No Active Reference
Refresh
ID
REF_ID
MOL_CELL
STAGE
ORGAN
TISSUE
387
18
New
Delete
Active ID -
Reference
Developmental Stage
A/C
Del
Cell Line
Organ
A/C
Del
Molecules per Cell
Tissue
A/C
Del
Expression Defined By
Cell Type
A/C
Del
Accept
Search
Cancel
Exit

5330

Fig. 32

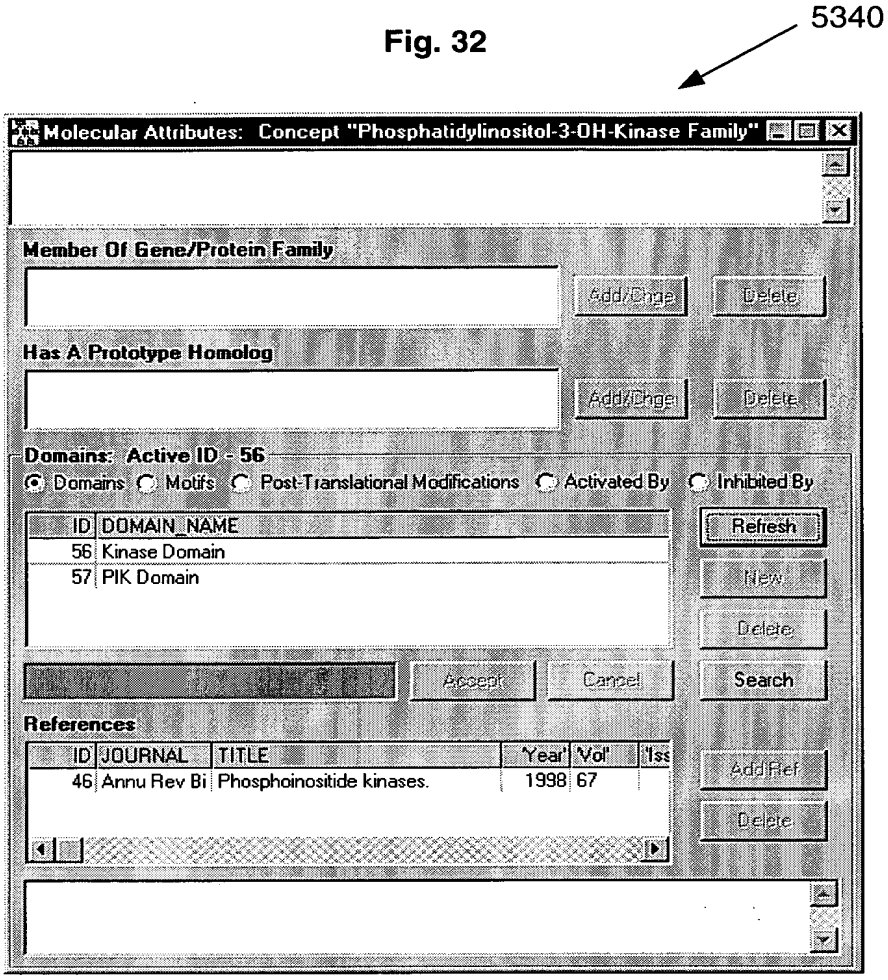
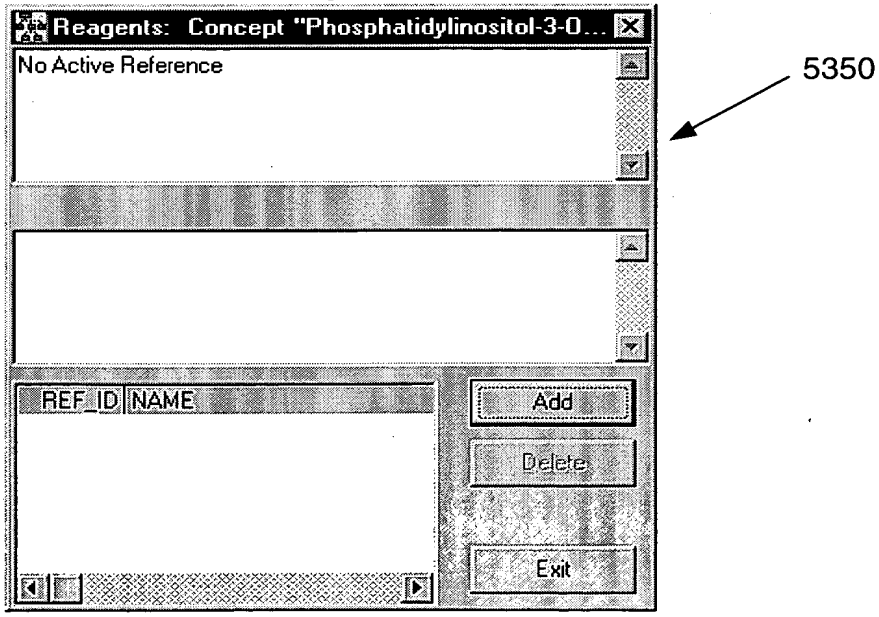

5340
Molecular Attributes: Concept "Phosphatidylinositol-3-OH-Kinase Family"
Member Of Gene/Protein Family
Add/Chge
Delete
Has A Prototype Homolog
Add/Chge
Delete
Domains: Active ID - 56
Domains
Motifs
Post-Translational Modifications
Activated By
Inhibited By
ID DOMAIN_NAME
56 Kinase Domain
57 PIK Domain
Refresh
New
Delete
Search
Accept
Cancel
References
ID JOURNAL TITLE Year Vol Iss
46 Annu Rev Bi Phosphoinositide kinases. 1998 67
Add Ref
Delete

Fig. 33


Reagents: Concept "Phosphatidylinositol-3-O...
No Active Reference
5350
REF_ID NAME
Add
Delete
Exit

5360

Fig. 34

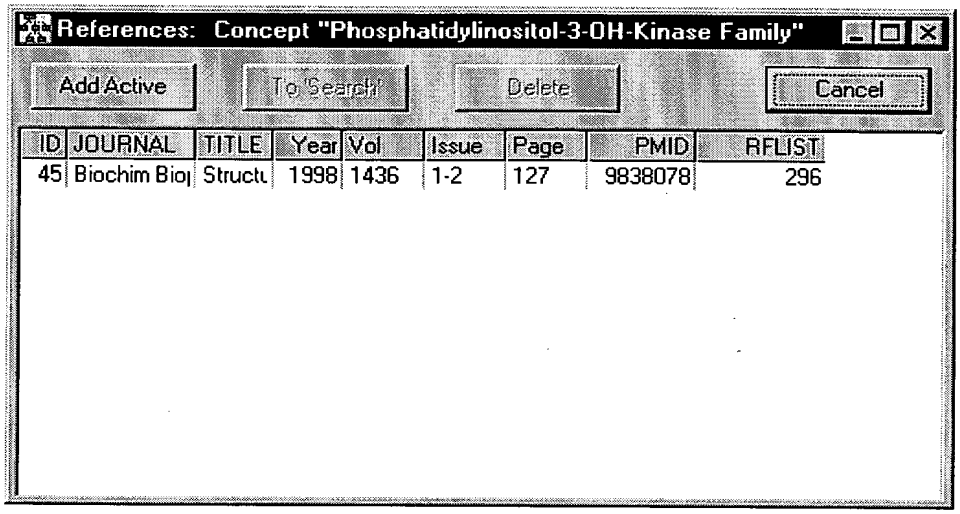
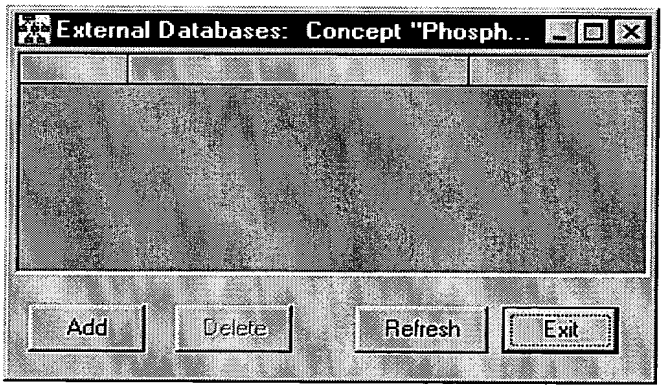


Fig. 35



5370

5380

Fig. 36

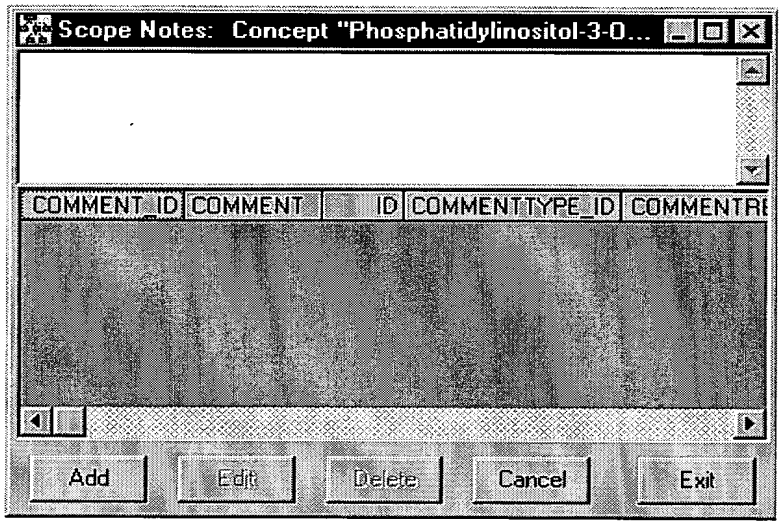
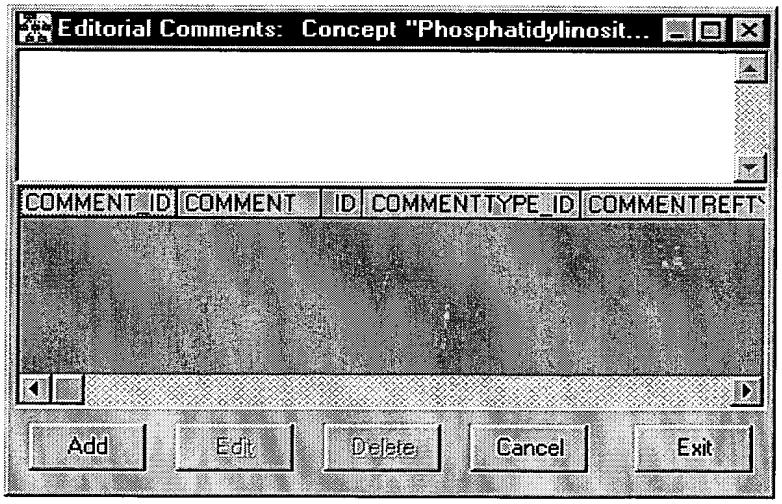
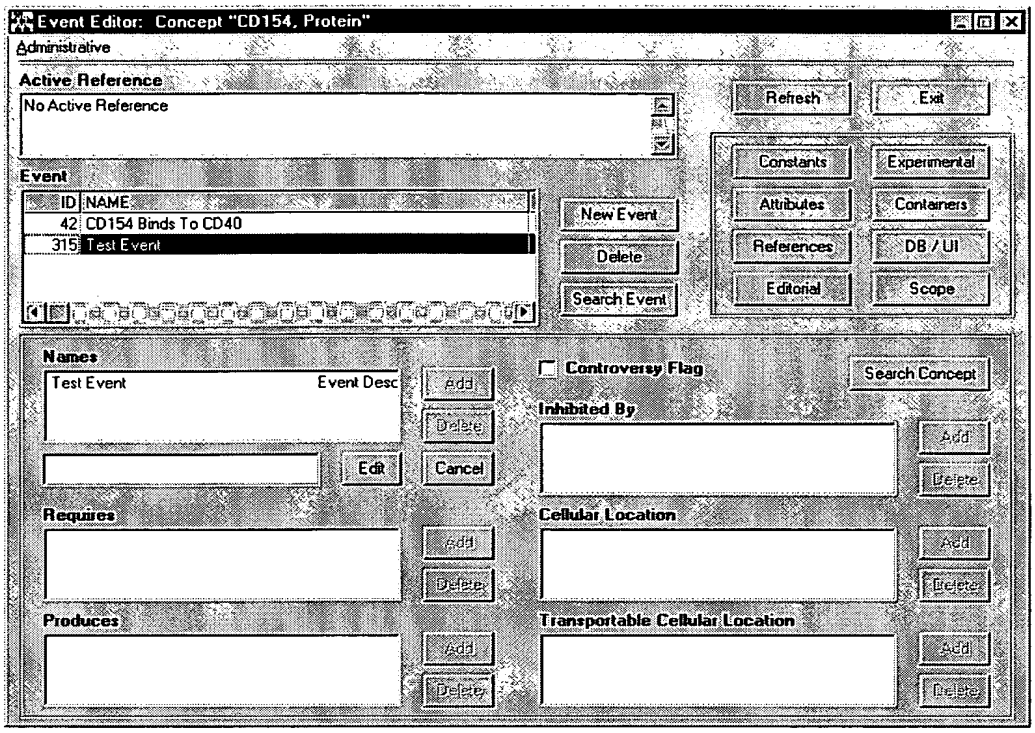


Fig. 37



5390

Fig. 38



5400

5405

Fig. 39

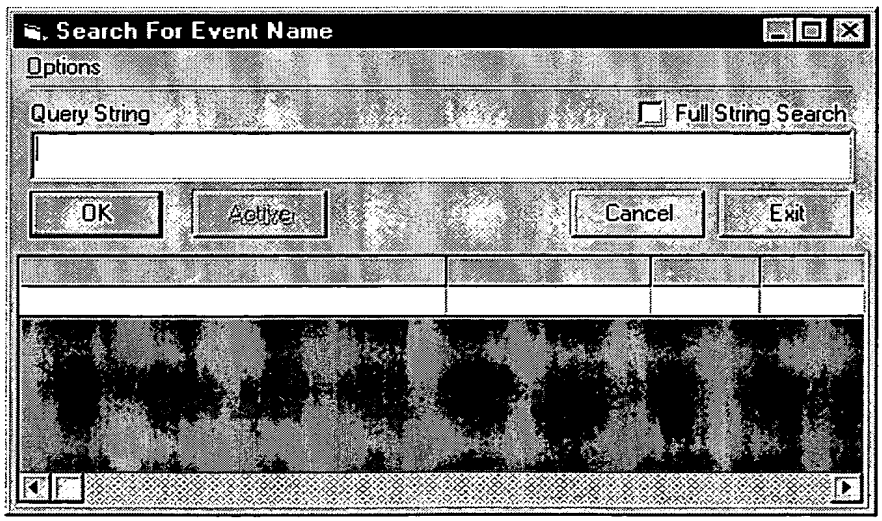
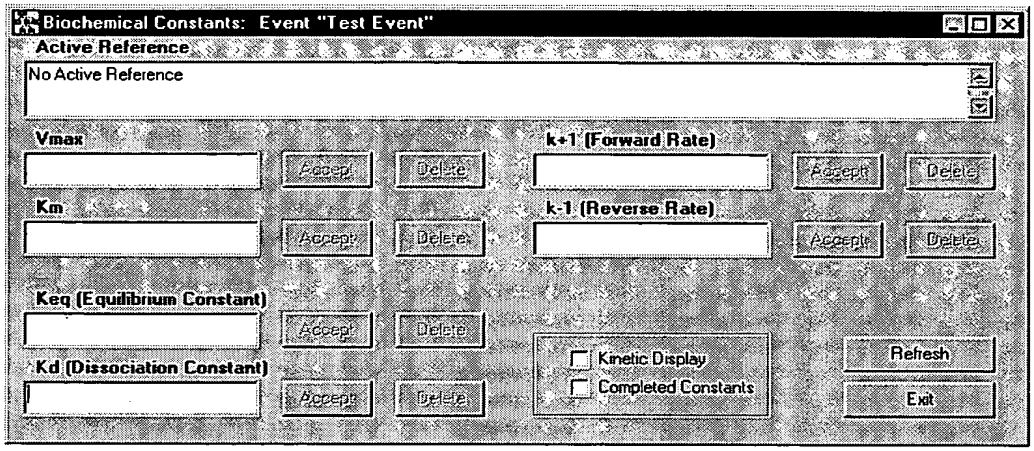


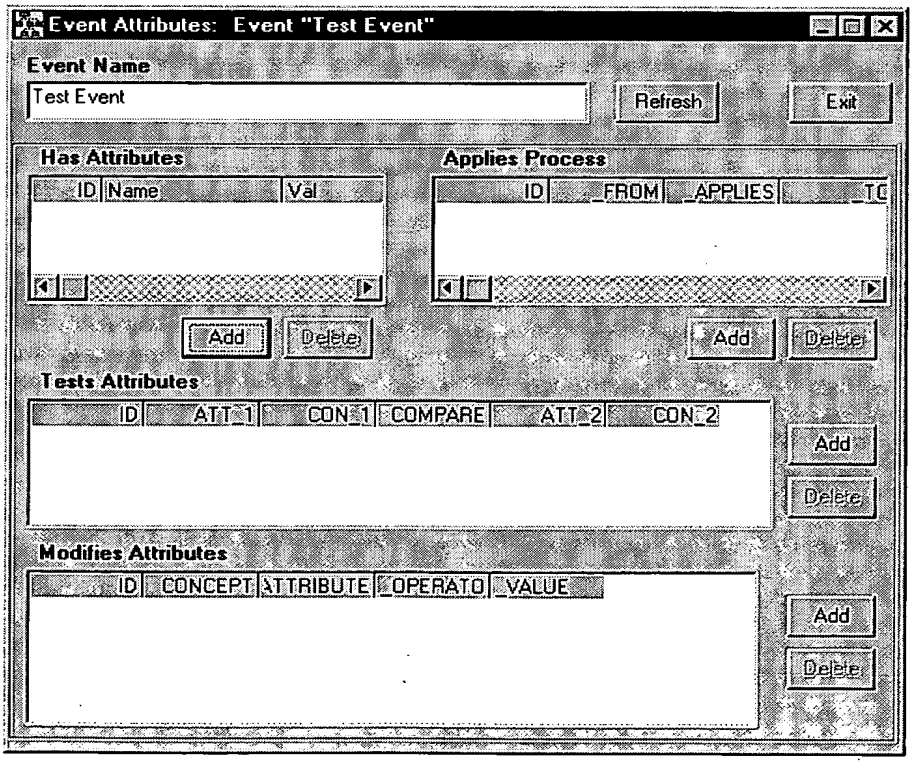
Fig. 40



5410

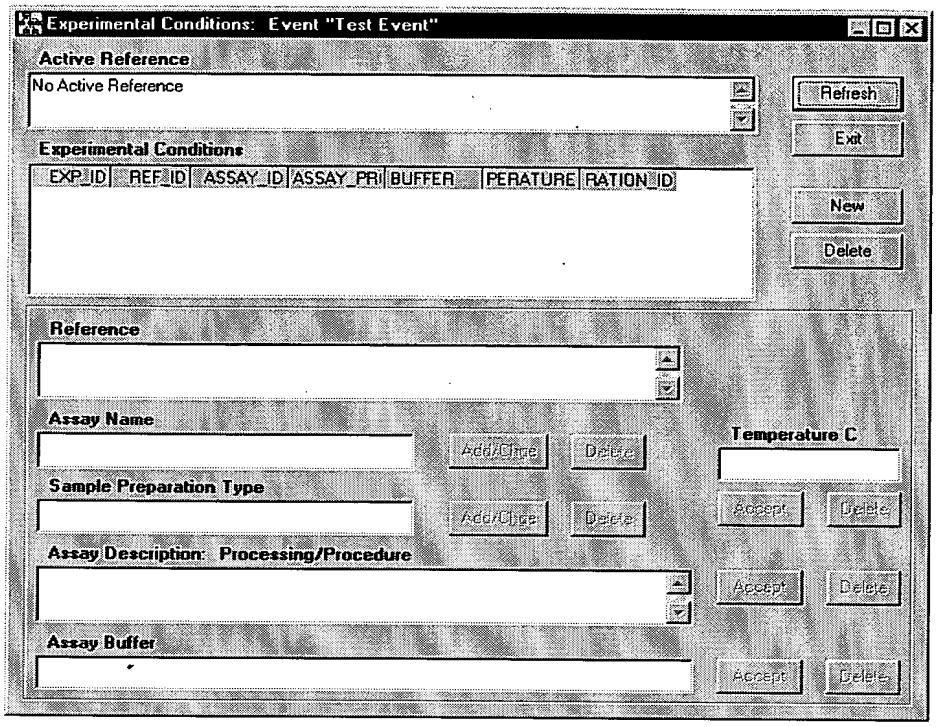
5420

Fig. 41



5430

Fig. 42



5440

Fig. 43